

SARTONIANA

Volume 22

2009

**Sarton Chair of the History of Sciences
University of Ghent, Belgium**

SARTONIANA

Volume 22

2009



Editors: R. Rubens and S. Dupre

**Sarton Chair of the History of Sciences
University of Ghent, Belgium**

© Academia Press

Eekhout 2

9000 Gent

T. (+32) (0)9 233 80 88

info@academiapress.be

F. (+32) (0)9 233 14 09

www.academiapress.be

De publicaties van Academia Press worden verdeeld door:

J. Story-Scientia nv Wetenschappelijke Boekhandel

Sint-Kwintensberg 87

B-9000 Gent

T. 09 255 57 57

info@story.be

F. 09 233 14 09

www.story.be

Gent, Academia Press, 2009, 130 pp.

ISBN 978 90 382 1516 7

D/2009/4804/212

U1360

Opmaak: proxess.be

Niets uit deze uitgave mag worden veeelvoudigd en/of openbaar gemaakt door middel van druk, fotokopie, microfilm of op welke andere wijze ook, zonder voorafgaande schriftelijke toestemming van de uitgeverij.

Table of Contents

Introduction	5
Laudatio Jens Høyrup	9
Erik Weber & Albrecht Heeffer	
State, “Justice”, Scribal Culture and Mathematics in Ancient Mesopotamia	13
Jens Høyrup	
Baroque Mind-set and New Science	47
A Dialectic of Seventeenth-Century High Culture	
Jens Høyrup	
Laudatio Pia Letto-Vanamo	75
M. Maresceau	
Law, History, and European Integration	79
Pia Letto-Vanamo	
Laudatio Paul Eling	87
Robert J. Hartsuiker	
Aphasia: where and how	91
Paul Eling	
Laudatio Maurice Lamy	111
Eric Mortier	
Current status of oxygen carriers	113
M. Lamy, G. Deby Dupont	

Authors

- Prof. dr. E. Weber. Faculteit Letteren en Wijsbegeerte, Blandijnberg 2, B-9000 Gent, België.
- Prof. dr. A. Heeffe. Faculteit Letteren en Wijsbegeerte, Vakgroep Wijsbegeerte en Moraalwetenschap, Blandijnberg 2, B-9000 Gent, België.
- Prof. dr. J. Høyrup. Roskilde University, Universitetsvej 1, P.O. Box 260, DK-4000 Roskilde, Denmark.
- Prof. dr. M. Maresceau. Faculteit Rechtsgeleerdheid, Vakgroep Europees gemeenschapsrecht, Universiteitsstraat 4, B-9000 Gent, België.
- Prof. dr. P. Letto-Vanamo. University of Helsinki, P.O. Box 44 (Jyrängöntie 2) FI-00014, Finland.
- Prof. dr. R. J. Hartsuiker. Faculteit Psychologie en Pedagogische Wetenschappen, Vakgroep Experimentele Psychologie, Henri Dunantlaan 2, B-9000 Gent, België.
- Prof. dr. P. Eling. Radboud Universiteit Nijmegen, Faculteit der Sociale Wetenschappen, Montessorilaan 3, 6525 HR Nijmegen Nederland.
- Prof. dr. M. Lamy. Centre Hospitalier Universitaire de Liège, Domaine Universitaire du Sart Tilman, Bâtiment B 35, B-4000 Liège 1, België.
- Prof. dr. E. Mortier. Faculteit Geneeskunde en Gezondheidswetenschappen, De Pintelaan 185, B-9000 Gent, België.
- Prof. dr. G. Deby Dupont. Université de Liège – Centre de l'Oxygène, Recherche et Développement, Institut de Chimie, B6a, Domaine Universitaire du Sart Tilman, B-4000 Liège, Belgique.

Introduction

When George Sarton wrote his History of sciences it became soon the standard textbook with the integration between the so called β sciences and α sciences. In his time the separation was already present but the divorce with estrangement had not yet occurred.

Now about one century later we can no longer speak from a divorce but a different world with a forceful apartheid being apparent. Just as apartheid luckily never succeeded we still have the presence even nowadays of research and technique from the opposing field in both scientific worlds. The quest for human knowledge is permanent and in the 21th century a unique stem still remains.

Based upon the mission of our university and to be faithful to the legacy of George Sarton a very important alumnus of Gent University we are proud to present here again the lectures of the Sarton Chair for the history of sciences.

First we have two papers by Jens Hóyrup about the importance of mathematics in the history of human thought. The mayor importance of mathematics even in the definition of baroque is certainly an eye opener. The second paper approaches the necessity of mathematics for the running of the state even in the oldest cultures known to mankind.

The contribution by prof. Pia Letto-Vanamo about one European history reflected in the unique axis of a common culture now accentuated by the development of a federal European Law makes it possible to evolve from the patchwork of nations to one common goal as set out so many years ago by Monnet.

The analysis of history of the aphasia is certainly an important field wherein the integration between the humanities and medical science was necessary to be able to help the very vulnerable people suffering from this

deficit in communication. It outlines in itself the obligation to observe the “mens” in every “corpus” notwithstanding the positivist credo.

Finally the paper from Lamy and Deby-dupont stresses how progress in biology and chemistry can help to perform life saving surgery.

R.Rubens

Chairman Sarton committee.

SARTON CHAIR LECTURES

Laudatio Jens Høyrup

Erik Weber & Albrecht Heeffer

Jens Høyrup was born in Copenhagen in 1943. He studied physics and mathematics at the Niels Bohr Institute of the University of Copenhagen and at the Institut Henri Poincaré of Paris University. In 1969 he obtained his master's degree. From 1971 till 1973 he was assistant lecturer at the Danish Academy for Engineering (Danmarks Ingeniørsakademi), where we taught courses in physics. In 1973 he became senior lecturer (and later on, in 1989, reader) at Roskilde University. He started in the Department of Social Sciences and ended up in the Section for Philosophy and Science Studies. Since 2005 he is emeritus. Since his retirement he publishes more books and articles and he attends more congresses than ever before.

His main field of teaching was the history of the natural, human and social sciences. His main field of research was, and still is, the history of science, especially the history of mathematics in pre- and early Modern cultures. He has studied the Babylonian, ancient Greek, Latin, medieval Islamic mathematical traditions, and – more recently – the 14th and 15th century Italian abacus tradition. Taken together, his research covers 3000 years of history of mathematics.

Jens Høyrup is a full member of the *Académie Internationale d'Histoire des Sciences*, is associate editor of *Historia Mathematica* and member of the editorial board of *Revue d'Histoire des Mathématiques*. He is a regular reviewer for several journals and publishers in the history of mathematics. He has published approximately thirteen books as author or co-author, about sixty articles in journals, about forty articles in conference proceedings and other books, and several contributions in encyclopaedic works. But of course, these numbers are not the reason why he has been proposed

for the Sarton chair and medal. Jens Høyrup has made many important contributions to the history of mathematics, and is responsible for many new insights and the revision of several once popular views. Let us give an overview.

His book *Lengths, Width, Surfaces: a Portrait of Old Babylonian Algebra and its Kin*, published in 2002 by Springer in New York, is on the one hand a typical example of history of science in the classic tradition of Heiberg, Tannery and Vogel: original texts are carefully reconstructed, translated and interpreted. On the other hand, Høyrup successfully provides new frameworks for interpretation and points to parallels between different traditions. Because of his command of more than ten languages, Høyrup often manages to establish links and develop etymological arguments which result in surprising new insights with respect to sources that have been analysed by several other scholars. This is also the case for this book. In order to study Babylonian clay tablets, he learned basic Akkadian and the essentials of Sumerian. The command of these languages enabled him to develop a revolutionary new interpretation: Babylonian algebra is based on geometrical methods used by lay surveyors. This interpretation is radically opposed to the classical interpretation of Otto Neugebauer. Neugebauer and his peers made the methodological choice to reach a “first approximation” to the terminology by applying modern mathematical conceptions to the texts. They found the formulae they were looking for and ignored small anomalies in the text referring to non-mathematical operations such as “laying down”, “breaking” or “to tear out”. Adopting the sound methodological principles of structural analysis and close reading Høyrup demonstrated that these terms refer to cut-and-paste geometrical operations of surveyors. Because there are no figures on the Babylonian clay tablets, such an interpretation was never considered before. It is an instructive lesson how to take distance from our modern conceptions while doing history and to discern conceptions different from ours. To put it in Høyrup’s words: “It is definitely easier to recognize which part of *our* mental luggage is absent from the Babylonian mind than to identify ingredients of this foreign thinking that are absent from ours”.

His book *Jacopo da Firenze’s Tractatus Algorismi and Early Italian Abbacus Culture*, published in 2007 by Birkäuser in Basel, contains many important new insights about the abacus tradition. Conventionally, this

tradition is considered to originate in Leonardo Fibonacci's *Liber Abbaci*, written in 1202. On the basis of a transcription of the earliest abbasus text, Høyrup argues that the tradition is older, has its roots in the Provence and Northern Spain rather than Italy, and that it is much less directly influenced by the scholarly level of Arabic mathematics than generally thought. The book on the abbasus tradition not only provides important new insights, it also illustrates how Høyrup's methodology differs from that of many other historians of science. He pays a lot of attention to what he calls the sub-scientific tradition, which includes the transmission of knowledge from master craftsmen to apprentices and social processes like the transmission of problems in practical geometry, recreational mathematics and their solutions. Historians of science tend to focus on "the big books" and neglect the other modes of knowledge transmission.

The Sarton chair was established in November 1984, at the centenary of Sarton's birthday, for which occasion a large conference was held in the very same building we are in today. Jens Høyrup was present at that conference with an early contribution on mathematics in medieval Islam. In the introduction to his latest book he kindly recalls the impressive talk given by Joseph Needham during the conference dinner calling him "my only teacher in the history of science". It is with great pleasure and honour that we can invite Høyrup again in these beautiful surroundings of Het Pand and hope that Høyrup will be an inspiration for a new generation in the same way he found inspiration in scholars as Needham.

State, “Justice”, Scribal Culture and Mathematics in Ancient Mesopotamia

Jens Høyrup

jensh@ruc.dk

<http://www.akira.ruc.dk/~jens>

Abstract

The functioning of the modern state presupposes a variety of mathematical technologies – accounting, statistics, and much more. Mathematics, on its part, needs the institutions of the state (schools, universities, research institutions, etc.) to secure financing, recruitment and the rearing of competence. At a given moment, the state as well as mathematics largely take the partner “as it is”, and none of them appears to the immediate view to depend for its essence on the other.

At the moment of pristine state formation, the situation was different. Most pristine state structures depended on organized violence, on religious institutions, etc., and mathematics did not enter. At least one major exception to this rule can be found, however: the earliest “proto-literate” state formation in Mesopotamia of the late fourth millennium, intimately connected to a system of accounting that seems to have guaranteed an apparent continuation of pre-state “just redistribution”. Both for its functioning and its legitimization, the state depended on the mathematics of accounting. On its part, the kind of mathematics which was created was totally bound up with its administrative role.

The lecture follows the interaction of state, “justice”, mathematics and scribal profession from the late fourth millennium over the “Ur III” period (21st century BCE, culmination and apparently end of the intertwinement of statal structure and legitimization with mathematics) until the Assyrian empire of the earlier first millennium.

State and mathematics

The functioning of the modern state presupposes a variety of mathematical technologies – accounting, statistics, and much more. Mathematics, on its part, needs the institutions of the state (schools, universities, research institutions, etc.) to secure financing, recruitment and the rearing of competence. At a given moment, the state as well as mathematics largely take the partner “as it is”, and none of them appears to the immediate view to depend for its essence on the other.¹

At the emergence of the state as a type of social organization, the situation was different. Most statal systems have originated in complex processes, either as “pristine states” via expanding chiefdoms or as “secondary states” in interaction with (often, indeed, as military protection against) existing states. As a rule, the involvement of anything than can be considered as mathematics in such processes has been peripheral, if not totally absent.

In a few exceptional cases, however, mathematical technologies have played a major role in the shaping of the state (and have, in consequence, themselves become more sophisticated in the process, developing into recognizable *mathematics*).

One instance of such an intimate bond is that between the Inca state and its accounting. I know too little about the matter to go into details – I suspect, moreover, that available evidence on the topic is insufficient to trace the connections between the development of the state and that of the *quipu* system.

Possibly, another instance is constituted by the relation (which, however, may be less pivotal) between the Maya states and their “chrono-theology”; even here I abstain from further discussion for lack of deeper knowledge.

In any case, the Maya state formation was not pristine.

¹ Second thoughts should force us to admit that this “immediate view” may not correspond to the actual situation of the latest four decades or so: without information technology, the immense increase of administrative control of citizens (to mention but that) would never have been possible. Only by discarding computer science from what we perceive as “mathematics” can we claim that the global mathematical enterprise has not been transformed in the same process. But this is not my topic here. I shall leave it to the reader to ponder after finishing the paper whether, paradoxically, the late fourth millennium BCE offers an illuminative model of our own lifetime. That possibility is indeed one of my reasons for choosing the subject I do deal with.

A third instance, perhaps the most indisputable case and at least the one which is best reflected in the sources (though still indirectly), is offered by the formation of states in southern Mesopotamia from the late fourth millennium BCE onward.

Prolegomena

Before approaching the subject-matter itself, something must be said about what I mean here by “mathematics”, and about the notion of a “state”.

For the present purpose, the transition to “recognizable mathematics” may be characterized as

the point where *pre-existent but previously independent* mathematical practices are coordinated through a minimum of at least intuitive understanding of formal relations.

Political anthropologists have discussed the emergence of *statal organization* of society in different terms, not necessarily as mutually exclusive as often assumed in the debate. According to Morton Fried’s classic *The Evolution of Political Society* [1: 235], the state arises as

a collection of specialized institutions and agencies, some formal and others informal, that maintain an order of stratification,

“stratified society” being a society [1: 186]

in which members of the same sex and equivalent age status do not have equal access to the basic resources that sustain life.

This stratification may come about in several steps: in brief, from “big man” practice to chiefdom spurred by warfare, leading to a three-class division *slave owners – commoners – slaves*.

Elman Service’s emphasis in the equally classic *Origins of the State and Civilization* was different, seeing [2: 305] *statal organization* as the end result of a quantitative and often gradual development from

relatively simple hierarchical-bureaucratic chiefdoms, under some unusual conditions, into much larger, more complex bureaucratic empires.

The chiefdom itself was understood by Service as a hierarchical organization legitimized by social *functions* wielded by the chief for common benefit² in a theocratic frame of reference, where

economic and political functions were all overlaid or subsumed by the priestly aspects of the organization.

A number of other, less abstract discussions of the early state have been regionally focused (either explicitly or implicitly). In an article on “Population, Exchange, and Early State Formation in Southwestern Iran”, Henry T. Wright and Gregory A. Johnson tried to base themselves “on the total organization of decision-making activities rather than on any list of criteria”, describing the state [3: 267]

as a society with specialized administrative activities. By ‘administrative’ we mean ‘control’, thus including what is commonly termed ‘politics’ under administration. In states as defined for purposes of this study, decision-making activities are differentiated or specialized in two ways. First, there is a hierarchy of control in which the highest level involves making decisions about other, lower-order decisions rather than about any particular condition or movement of material goods or people. Any society with three or more levels of decision-making hierarchy must necessarily involve such specialization because the lowest or first-order decision-making will be directly involved in productive and transfer activities and second-order decision-making will be coordinating these and correcting their material errors. However, third-order decision-making will be concerned with coordinating and correcting these corrections. Second, the effectiveness of such a hierarchy of control is facilitated by the complementary specialization of information processing activities into observing, summarizing, message-carrying, data-storing, and actual decision-making. This both enables the efficient handling of masses of information and decisions moving through a control hierarchy with three or more levels, and undercuts the independence of subordinates.

² According to Service mostly functions of a redistributive nature; but if we include functions of military leadership the contrast with Fried can be seen to be far from absolute.

Though meant to be generally useful, the description *was* specifically geared to what happened when statal systems emerged in southern Mesopotamia and southwestern Iran, for which reason I shall adopt it here.

The West-Asian “token system”

Central to the “control” which Wright and Johnson spoke about is the “token system”, an accounting system based on small and less small cones, spheres, discs, tetrahedra, rods etc. made of burnt clay – often (though at first only rarely) provided with markings that define sub-types. The system turns up in Syria and Western Iran around 8000 BCE, concomitantly with the agricultural revolution, spreading over the following millennia to a region reaching from south-eastern Anatolia and Palestine to the Iranian plateau, and remaining alive at least until the early third millennium BCE. Though some suggestions had been made in discussions of late fourth-millennium Iranian material, the discovery of the system and of its chronological and geographical range is unambiguously the merit of Denise Schmandt-Besserat. Her first publication on the topic [4] is from 1977; a complete survey of her results and interpretations is the double volume *Before Writing* [5].

According to their use in the fourth millennium and to continuity with proto-cuneiform writing, the various tokens served to represent quantities (presumably standard containers) of grain, oil, etc., and heads of livestock – perhaps also quantities of work.

For a number of reasons, the original social function of the system cannot have been inter-community trade (which did exist, as documented by the spread of obsidian). First of all, any use of quasi-monetary symbols without tangible value (paper money, bills of exchange) presupposes banks and police forces which can enforce the obligations they represent. Moreover, the tokens were simply thrown out once they had been used, which excludes even a local monetary function.

Instead, the use of prestige versions (made from marble, alabaster, etc.) as grave-goods in high-status graves [6] and the presence of tokens in communal storehouse areas suggest that the tokens functioned as means of accounting in a redistribution system, and that management of this redistri-

bution system carried very high social prestige – cf. Elman Service as quoted above.

In this connection, two observations should be made:

- Redistribution within the community is very common in pre-state societies, but redistribution built on detailed accounting is rather unique. If Inuit hunters kill a walrus and give others access to the meat, this is done from an expectation of reciprocity, and on the part of the more skilled hunters in expectation of prestige; but in neither respect is detailed accounting involved, nor possible.
- Accounting by means of tokens can doubtlessly be characterized as a *mathematical technique*. But we have no evidence for numerically standardized bundling of units (actually there is some counter-evidence from the fourth millennium, cf. below). It is therefore most likely that (e.g.) a small cone corresponded to a specific customary basket containing grain and a small sphere to some larger equally customary container, and that the ratio between the two was not numerically but physically (that is, not precisely) fixed. In other words, the mensuration inherent in the token system appears not to have been coordinated neither with the bundling levels of an oral counting system nor with any other numerical bundling principle; if this is so, the system is hardly an instance of (integrated) *mathematics* in the above sense.

Fourth-millennium developments

In the earlier fourth millennium, the city Susa in a river valley in the Zagros area in southwestern Iran became the centre of a wider settlement system; in this context the redistribution system developed into what looks most of all as payment of tribute or taxes to the central temples of Susa. The tokens were put to new use: enclosed in hollow clay envelopes (“bullae”), they appear to have served as bills of lading for goods delivered from the periphery to the centre. This goes hand in hand with the development and refinement of other bureaucratic devices and procedures – not least the use of cylinder seals as “certifiable signatures” of particular officials or offices. Since the contents of bullae could only be “read” if they were broken (after which they could no longer be controlled), impressions (or representative

pictures) of the tokens to be put into them began to be made on their surfaces before they were closed and sealed.

A somewhat similar social development may have started slightly later in Uruk in the Mesopotamian South, but it soon went much further. The background was that a climatic change and lowering of the water level in the Gulf opened the possibility for irrigation agriculture in the future Sumerian area, allowing a violent growth of agricultural output as well as population – see, e.g., [7: 58-61].

Probably in an initial phase, it was realized that impression or depiction of the tokens on the surface of bullae made it possible to dispense with the contents, and that the bulla itself could then be replaced by a flattened piece of clay as carrier of the impressions/depictions.³ Very soon (c. 3200 BCE⁴), writing was also invented – *invented* indeed, in one leap or at least in a very speedy process (no “primitive” precursor steps are known).⁵

The “proto-literate” script was ideographic, and used composition in a way that is quite similar to what is found in pidgin and creole languages.⁶ Most signs (traced by means of a pointed stylus) were directly pictographic, showing for instance a jar, a head, the mountains to the east, the sun rising between these, etc.⁷ Some, however, depict *tokens representing the thing* instead of the thing itself. Quite striking, and enigmatic until the discovery of the token system, is the sign for a sheep: a circle marked by a cross. Indeed, it does not depict the animal but the token standing for the animal.

³ These “numerical tablets” provide the evidence referred to above that no arithmetically defined bundling system was yet in existence around the mid-fourth millennium BCE.

⁴ From this point onward, I follow the “middle chronology”, as used, e.g., in [8]. It should be pointed out that dates, even when they can be given exactly *within* this chronology, are not fixed absolutely before the first millennium BCE.

⁵ Except for what will be said about the possible existence of a creole language, most of what is said in the following about early writing and accounting and their function is explained in much greater depth in [9]. In general, I draw heavily on the works of Hans Nissen, Peter Damerow and Robert Englund.

The reconstruction of underlying cognitive type and mathematical conceptions are on the whole of my own responsibility.

⁶ This statement should not be taken as a claim that the inventors of the “proto-literate” script spoke a pidgin – the patterns in sacred architecture shows cultural continuity over about 2000 years preceding the invention, and thus continuity of the culturally hegemonic stratum of the area. But the principles of the invention *may* have been inspired by familiarity with a pidgin spoken by enslaved populations – cf. *imminently*.

⁷ In the third millennium, the drawings were no longer traced but made by oblique impression of a prismatic stylus; this gave the script its characteristic “cuneiform” character. The early as well as the developed forms are shown in [10].

In contrast to these drawings of things or tokens, metrological and numerical units were *impressed* by a different stylus, as representations of tokens. This stylus was cylindrical, thick in one end and thin in the other. Impressed vertically it might produce a large or a small circle, oblique impression could represent a large or a small cone.

The proto-literate script did not attempt to render the sentences of spoken language – it was not “glottographic”. Some 85% of the surviving texts are accounts made in fixed formats, rather to be likened to a statistical table or a ledger than to literary texts; what was written could of course be *spoken of or told* in words but it could not be *read*. The remaining 15% are “lexical lists” which served to teach the script.

Whereas writing was thus (to all we know) invented in Uruk, the idea and the bureaucratic use (not the script itself) were soon borrowed into Susa and a number of other Iranian localities which formed a shared cultural system. Until some decades ago the earliest known evidence for Egyptian writing was a century or two later than the earliest Uruk script, and contemporary with artefacts inspired or imported from Mesopotamia (e.g., cylinder seals). It therefore seemed a good guess that even the Egyptian script was inspired by knowledge of the *possibility* to write (whatever that may mean precisely); now, as the earliest beginnings of Egyptian writing has moved back a century, this is much more doubtful [11]; independence seems more likely, but partial inspiration going either way cannot be excluded.

The proto-literate Uruk metrologies

In the numerical and metrological sequences of the Uruk writing system, bundling was numerically determined.⁸

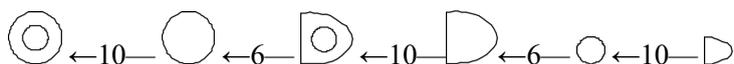
One sequence was used for the measurement of grain, and may reasonably be considered a continuation of the traditional use of tokens. The “basic unit” in this system, depicting a small cone, was . 6 of these became , the picture of a small sphere. 10 small spheres were , the picture of a

⁸ For the following description of the metrological and numerical sequences I build on [12].

large sphere. 3 large spheres were bundled as , the picture of a large cone. 10 large cones, finally, became , possibly a representing a punched large cone (an existing token), but perhaps a new construction made in parallel with the number sequence. In a notation due to Jöran Friberg, the sequence as a whole looks as follows



Another sequence was used for counting most types of discrete items, and may be regarded as a “number sequence”. Whereas the grain sequence is likely to continue an old system in a new medium (though now with arithmetical bundling), the number sequence can be supposed to be new – the representation of pure numbers (that is, numbers abstracted from the quantity they count) by tokens will have had no purpose, at least not before their inclusion in bullae (here, the external official’s seal might *in principle* determine which kind of goods was involved). The corresponding diagram is

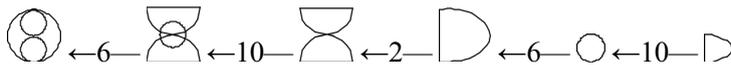


This sequence, in contrast to the preceding one, is highly systematic, and therefore almost certainly represents a deliberate transformation of the grain sequence made so as to fit an existing oral number system, and perhaps extending it beyond existing spoken numerals. As we see, the signs for 600 () and 36000 () are produced by superposition of 10 () on 60 () and 3600 (), respectively, while 60 () is chosen as an “enlarged” unit ()

The latter feature suggests that the spoken numeral system treated the step $1 \rightarrow 10$ differently than the step $10 \rightarrow 60$ (if not, there would be no reason to invert the order of  and  in the grain system); 60 must in some way have been understood as a “return of the unit”. Evidently, the “second return” of the unit as 3600 could not repeat the visual trick, the “number-and-measure” stylus having only two ends, each of which could be

impressed vertically or obliquely. In consequence, the written system gives no clues as to whether 3600 was already a unit in the spoken system.

For specific counting purposes – apparently the counting of bread or grain rations, perhaps also portions of dairy products – a particular “bi-sexagesimal system” with the following structure was in use:

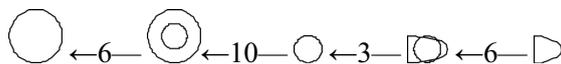


The agreement with the lower orders of the “general” counting system suggests the bisexagesimal system to have been shaped so as to fit particularly bureaucratic procedures or habits. Such an adaptation recalls our counting sheets of paper in units of 500, bottles of wine in dozens, etc., sometimes but not always corresponding to standard packages – such adaptations are amply present in the later Mesopotamian record.

We might be tempted to conclude from the divergence of the two counting systems after the level of 60 that the level 3600 did not exist in the spoken number system but was a product of the new bureaucratic device; the existence of the medieval “hundredweight” and the Germanic *Großhundert*, both deviating from the pre-existing 100 for similar reasons, shows that such a conclusion is not warranted.

Two other metrological sequences exemplify the converse process, the adjustment of administrative procedures to mathematical structures. One is the area system, the other the administrative calendar.

The structure of the area system in itself shows little mathematical system:



Such lack of mathematical system is in itself an indication that the system is a normalization of a pre-existing system of “natural” (irrigation, seeding or similar) measures – a conclusion which is supported by linguistic arguments [13, *passim*]. There is no direct proof of it, but it is a fair assumption that the system (which coincides with what is still known and well documented in much later periods) was already geared to the length metrology (based on the unit *nindan* or “rod” of c. 6 m) – not least since it is almost certain that the area of slightly irregular rectangular fields was already

determined as average length times average width (the “surveyors’ formula”), which would make no point if area units were not derived from length units. \square (the iku of later times) would then be the square on 10 nindan, \square a rectangle contained by 10 and 60 nindan.⁹ On this foundation we may conclude that the area metrology presents us with a deliberate coordination of several mathematical techniques and with integration of the result in the administrative procedures concerned with the allotment of land in arithmetically determined proportion (which, without this new tool, could not be made, and hardly imagined).

Alongside the true luni-solar calendar with its months of variable length and its insertion of intercalary months when such turned out to be needed (which remained in use for ritual and time-keeping purposes until the first millennium BCE), an administrative calendar was introduced, which counted each month as if it consisted of 30 days, and each year as 12 months¹⁰. It served for the calculation of fodder to be allocated to herds and, at least in later times, of the work which overseers were to press out of their crew each month irrespective of its length. Even in this case, only the introduction of a mathematical tool made possible the system of intense administrative control of subordinate staff.

Still other metrological sequences were in use – most of them derived from those already mentioned by means of various kinds of extra marks (similar to those that had served in the token system), and serving, for instance, to count malted instead of ordinary grain. There is no need to describe them in detail.

One common feature of all sequences which is worth mentioning is the way they were provided with subunits below \square . In all cases, the first level of sub-units was obtained by rotating either this sign or a shortened \square 90°

⁹ The definition of area units in terms of linear metrology presupposes a conceptualization of area linked to square and rectangular shapes with measured sides; that this conceptualization was at hand, however, is not subject to doubt. Firstly, a number of prestige buildings in the area from this and earlier periods exhibit clearly rectangular layout – a number of specimens are rendered in [14]; secondly, the dimensions at least of certain buildings from the proto-literate period are determined in terms of an identifiable length unit – see [15].

This modular-orthogonal architecture represents a kind of “integrated” mathematics beyond the one represented by the state-accounting complex.

¹⁰ This calendar and its use until the outgoing third millennium BCE was analyzed in depth by Robert Englund [16].

clockwise,  and , respectively –  standing apparently for a halving (except when a day is seen as a sub-unit of an administrative month),  for a division into 5 parts.

It is possible that *one* of these subdivisions precedes writing –  could well be a depiction of a hemisphere, one of the old tokens. But , a mere rotation of , can hardly correspond to a particular token, nor can a rotation possibly correspond to any feature of the token system. Globally, the way sub-units are formed thus reflects an underlying general idea of “forming sub-units”.

Another general feature to be observed has to do with the function of the counting sequence. As observed above, freely movable tokens had to represent both the *kind* of thing they stood for and the quantity involved. In writing, it became possible to separate the two, combining, e.g., the ideogram for a sheep with the number “2” – which was indeed done. The mental habit involved in this splitting of quality and quantity also underlies the way the “lexical lists” were constructed from which the script was learned: in Luria’s terminology [17: 48ff], it reflects “categorical classification” and not “situational thinking”. A plough will thus appear in a list of wooden objects, not together with the ploughman or the grain. In one list – the “profession list” – the Cartesian product is not only an external condition but also involved in the structure of the list itself, which confronts field of activity with the hierarchy of positions. Even the orderly formats of bureaucratic accounting reflects the same mental habit.¹¹

The splitting into a Cartesian product of quantity and quality was not followed rigidly: quality, if determined unambiguously by context, was routinely left implicit – if a number stood for the length or width quality of a field, the unit *nindan* was thus omitted. This should not be understood as an indication of “primitivity” but as an instance of economical flexibility of thought: exactly the same thing happened, for instance, when Stevin’s

¹¹ According to Mogens Trolle Larsen [18: 211], the format of the lists “points to a special logic that is additive and aggregative rather than subordinative and analytic”, and whatever hierarchy occurs in the list simply reflects “the surrounding highly stratified society”. In [19: 337] I endorsed this view, but second thoughts now suggest to me that the hierarchy of the “profession list” is too regular to represent a spontaneous historical development: it looks like a construction inspired by categorical thought, perhaps fully implemented in real social life, perhaps in part a theoretical construction reflecting how future officials were meant to perceive social reality.

decimal fractions came in common use, and his $375\frac{7}{12}$ was reduced to 375.72 .¹²

Even this principle of economy can be seen in the light of Luria's dichotomy: Situational thinking is the habit of those whose world is largely made up of fixed situations, categorical classification is needed by those whose existence is less predictable – but in situations that *are* predictable, there is no reason they (indeed *we*) should not resort to the simpler pattern. True mental flexibility encompasses the possibility to switch when it is adequate to subordinate patterns which, *if* they were hegemonic, would not be flexible.

Uruk: A “mathematical state”

If the emergence of mathematics proper is understood as the coordination of “*pre-existent but previously independent* mathematical practices [...] through a minimum of at least intuitive understanding of formal relations”, there is hence no doubt that mathematics had started its career, if not before, then at least in late preliterate or proto-literate Uruk (and Susa) – nor that it were primarily the needs of the administration of the new social system that asked for the creation or further unfolding of mathematics.

More interesting is perhaps the converse observation. The use of the mathematical tool was no instance of pure “technical rationality”, the creation and implementation of means for an already established end which itself is not touched. If we compare the Uruk and subsequent Mesopotamian state formations with other early states, the end itself (the Mesopotamian state) can be seen to have been shaped by the means, no less than the successful appeal to military means may lead to the transformation of the state that appealed to it.¹³

A rash statement of this kind must evidently be explained. Redistributive systems are found in many pre-state societies; they correspond to the need for mutual support, and may thus be said to correspond to a notion of social justice. However, this notion of justice cannot easily be carried over to the proto-statal situation. In Robert Carneiro's words [22: 58], “what a chief

¹² This theme is further explored in my [20].

¹³ Keeping aloof from real politics we may think of Kästner's nightmarish poem about what would have happened to Germany after WW1 “Wenn wir den Krieg gewonnen hätten” [21: 102/].

gets from redistribution proper is esteem, not power”; further on (p. 61) Carneiro observes that

As long as a chief merely returns everything he has been handed, he gains nothing in wealth or power. Only when he begins to keep a large part of it, sharing with his retainers and supporters but not beyond that, does his power begin to augment.

But the power of a chief to appropriate and retain food does not flow automatically from his right to collect and redistribute it. Villagers freely allow a chief to equalize each family’s share of meat or fish or crops through redistribution because they benefit from it. But they will not willingly suffer the same chief to keep the lion’s share of food for himself. Before doing this, he must acquire additional power, and that power must come from some other source.

Since power only results when redistribution proper (where the chief retains only a small percentage of what passes through his hands) is transformed into *tribute* or *taxation*, where he keeps a large part for himself and for the “core of officials, warriors, henchmen, retainers, and the like who will be personally loyal to him and through whom he can issue orders and have them obeyed” [22: 61], neither the commoners nor the chief and his circle have any immediate reason to conceptualize the new situation in terms of social justice.

In the Susa-Uruk area, matters were probably perceived differently (at least by upper and middle strata), even though realities may have been similar. As shown by the use of *bullae* and by the accounting tablets, taxation and allocation of resources – be it the fields apportioned to high-ranking temple officials, be it the rations of grain distributed to workers – were made according to mathematically determined rules. In this way, statal power was structured around “just measure” and thus, apparently, legitimized by a transformed concept of social “justice”. Since accounts and lexical lists constitute our only written sources, we have no direct evidence for how the situation was conceptualized at the time; but literary evidence from a time when lexical lists from the proto-literate period were still in use indicates that at least the higher literate stratum thought of statal power in such terms.

A striking contrast is offered by early Pharaonic Egypt, the “nearest neighbour” in terms of state formation. All evidence suggests that the Pharaonic

state was legitimized by conquest, and (at least in the view of the literate) by a religious guarantee of cosmic order. Already during the First Dynasty, it is true, the yearly level of the Nile was recorded, in all probability in order to allow calculation of the taxation level of the year to come, and a biennial “counting of the riches of the land” was introduced.¹⁴ But a biennial counting certainly does not allow any specific determination of dues and rights, nor is there any evidence that the measured Nile height served such purposes. Social “justice” has no place in the picture of early Pharaonic Egypt.

“Real justice”

“Real socialism” did not coincide too well with what had been proclaimed in programmes, and the real feudalism of the Middle Ages was conspicuously different both from Charlemagne’s blueprint and from Fulbert of Chartres’ theory of the respective roles of the praying, the warring and the labouring order. Likewise, mathematical social “jubstice” (however much unequal) was certainly not the whole truth about the Uruk state. But it remains an essential part of the truth, and it conditioned Mesopotamian statal structures at least until the mid-second millennium BCE.

That it was only *part* of the truth, belonging rather on the level of hegemonic ideology than on that of social realities, can be seen from the preferred motif of the seals of high officials (found on no less than half of all known early Uruk seals; two specimens are reproduced in [9: 16]): A high official or priest looking on while overseers beat up pinioned prisoners. It is probable that the vehement increase in population did not result from local breeding alone but also from enslavement of significant populations from the mountain areas to the east – the pictograms for male and female slaves are indeed composed of an indication of sex (of a person) with a picture of the mountains¹⁵ – and that this was brought about by the same climatic change as had made possible the irrigation revolution in the lowlands.

Such a hypothesis is supported by linguistics: many features of Sumerian look like those of languages that over some centuries have developed from

¹⁴ Nile observations as well as countings are documented on the Palermo Stone – translated, e.g., in [23: 67–95].

¹⁵ No. 50 and 558, respectively, in Labat’s sign list [10].

pidgins and creoles.¹⁶ Enslaved workers are likely to have had different languages – also in later times, many languages are found in the region. Like the slaves in the West Indian plantations (who were in the same linguistic situation), they can therefore be supposed to have created a pidgin (based largely on the vocabulary of the masters’ language but losing its grammar) which the next generation transformed into a creole.¹⁷ In the absence of a metropole conserving their original language, new generations of masters influenced as children by lower-class nurses and servants will also have adopted the creole over some generations (probably without perceiving the shift as a change of language) – the final outcome (after centuries) being Sumerian.¹⁸

The Early Dynastic and Sargonic periods

The proto-literate period may have lasted from c. 3200 BCE to c. 2900 BCE (falling in two distinct sub-periods, “Uruk IV”, 3200-3000, and “Uruk III” or “Jemdet Nasr”, 3000-2900). It was followed in the Sumerian area (now without doubt Sumerian) by the “Early Dynastic Phase” (subdivided into ED I, ED II and ED III), c. 2900-2750-2600-2350 BCE.

In this phase, what appears to have been a social system with one major centre (Uruk) changed (collapsed?) into one consisting of competing city states; and what looks like a state centred around a staff of high temple officials developed into states ruled by a king (though still heavily influenced by the temple institution).

From ED I we have no written sources, and from ED II very few. In ED III, their number proliferates; the continued use of the old lexical lists demonstrates continuity not only of the writing system but also of the school tradition. In the 26th century, however, a new phenomenon can be observed. Writing was now in wider use, serving also, e.g., for the stipulation of private contracts; at the same time, and in consequence, the circle of the

¹⁶ This theme is explored in depth in my [24].

¹⁷ For this process, see for instance [25] or [26].

¹⁸ Since the proto-literate script was ideographic and indicated neither grammar nor the word order of full sentences, we have no means to identify the language spoken by its inventors. One or two cases of possible use of homophones corresponding to later Sumerian (“rebus principle” writing) decide nothing, since a pidgin and the creole it engenders borrow most of their vocabulary from the language of the masters – cf. the derivation of the language name *Tok pisin* from (the pronunciation of) *talk pidgin*.

literate became broader; in John Baines' terms [27], a transition from "very restricted" to "restricted literacy" took place. The group of scribes (dub.sar) turns up for the first time as a distinct *profession* in the city-state Shuruppak [28: 4, 12-23].

Also at the same time, and in all probability as a further consequence of this, the script was put to new uses. We find the first literary texts – a proverb collection and a hymn – and the first instances of "supra-utilitarian" mathematical school problems (problems that are not directly connected to practice even though they are formulated as if they were). In contrast, all mathematical texts from the proto-literate period that can be identified as school texts are "model documents", distinguishable from real administrative texts only by the absence of an office seal and by the occurrence of numbers that are suspiciously round or nice and at times suspiciously large.

Literary texts as well as supra-utilitarian mathematics were probably meant to probe and make manifest the reach of the two professional tools – writing and computation – and thus as expressions of professional pride. This agrees well with the appearance of many of the so-called "school-texts" from Shuruppak (edition in [29]): empty corners may be filled out by nice drawings, and according to the judgement of Aage Westenholz (personal communication) the tablets may indeed be *de luxe* versions made for mature scribes looking back at the real or imagined pleasure of their school time, emblem of their present professional identity and social position.¹⁹

Rising city walls show clearly that warfare was an endemic condition of the ED-period, and that the king was a military leader; Shuruppak itself was completely devastated in a military attack, following upon a general mobilization [30: 144f]. The many killed servants that followed their master to the underworld in the Royal Cemetery of Ur (initial ED III) also demonstrate that the king had given up any idea of being the servant of society – he was its overlord, and society a means for his greatness. None the less, only the very end of the ED period gives us written evidence, if not of the ritual slaughter of servants then at least of military activities; until then, even royal inscriptions show the king solely as the benefactor of temples

¹⁹ Cf. Giuseppe Visicato's work on third-millennium scribes [30].

and provider of agricultural prosperity (in strong contrast to early Pharaonic documents). Literacy, so it appears, only reflects the functional and pseudo-just characteristics of the state; those features of the state which had been irrelevant for the invention of writing and bookkeeping remained outside the perspective of writing. In this respect, ED Sumer was a *dual society*, one of whose faces was still “mathematical”.

From c. 2350 to c. 2200 BCE, the Sumerian area (and soon the whole of Mesopotamia and even more) was united into a single territorial state; after an initial short-lived centralization around a Sumerian city-king, the centre was the Akkadian “Sargonic” state²⁰ (Akkadian is a Semitic language, of which the later Babylonian and Assyrian languages are dialects, Sargon the founder of the dynasty; the school language remained Sumerian).

“Literature”, at first apparently a free creation of the scribe school and a means for scribes to probe and demonstrate their professional identity, was soon taken over by the Sargonic rulers as propaganda (hymns being written so as to serve the new dynasty [31: 186]). While mathematical administration certainly expanded [32], the utilization of supra-utilitarian problems in mathematics teaching was continued; there is no reason to presume that they fulfilled, or could fulfil, any role outside the school.

Already during the ED phase (documented in ED III) but accelerating during the Sargonic period, metrologies were adjusted with concern for mathematical regularity as well as administrative convenience. The former concern (mathematical regularity) is especially visible in the weight system, apparently a fresh development of the ED phase, where the step factor 60 was given a prominent position (only one factor had to be 3×60 in order to accommodate the “natural” measure of a barleycorn). But other metrologies too were extended upwards and downwards with this step factor.

The concern for administrative convenience, at times but not always in conflict with the former, asked for the adaptation to administrative procedures or technical practice, for instance in the definition of a Sargonic “royal” gur (“tun” – the largest capacity unit) and in the creation of particular brick metrologies geared to the various standard bricks; cf. [28: 5] [33].

²⁰ Given the travelling times and the plurality of languages it is even justified to speak of an “empire”, as indeed often done.

All in all, the relation between the state and its mathematics seems to have developed during the later ED and the Sargonic period along lines known from other societies provided with an accounting or otherwise mathematically organized administration: mathematics was taught in a way which was needed by future staff, but it was also allowed a certain autonomy in the school. It was certainly not taught by “mathematicians” – but even when teachers are supposed to teach for practice, teaching will normally be affected by the fact that the practice which teachers are *really* familiar with is the practice of teaching. Thus also here, according to the meagre evidence at our disposition.

The Janus-faced innovations in metrology correspond to this tension in the situation of mathematics: sexagesimalization is likely to have been driven by a preference for intra-mathematical coherence, the other innovations by the links to extra-mathematical practice, in particular to the administrative procedures of the state.

The Neo-Sumerian state

Around 2200, the Akkadian territorial state or “empire” lost most – in the end all – of its territory, and smaller states reemerged, of which only Gudea’s Lagash (2141-2122 BCE) has left sources that might be considered relevant for our topic – inscriptions telling in meticulous accounting what he has given to the temple, and how he laid out the geometric plan for sacred buildings (texts with translation in [34: 69-101], see in particular pp. 72-82). From 2112 BCE onward, however, the Third Dynasty of Ur established a new “Neo-Sumerian” territorial state or empire, mostly referred to as “Ur III”.

The early decades of this dynasty present us with nothing spectacular. In 2074 BCE, however, king Šulgi undertook a military reform, which was immediately followed by an administrative reform. From this point onward and until the collapse of the empire, scores and scores of thousands of accounting tablets inform us about the details of the administration (and, indirectly, about its governing principles).

At least in the Sumerian South, the larger part if not the overwhelming majority of the working population in both agriculture and handicraft

production seems to have been submitted to conditions close to those of slavery,²¹ working in crews under scribal overseers who were responsible for the work performed, reckoned in units corresponding to $\frac{1}{60}$ of a working day (i.e., 12 minutes).

The accounts of the overseers are extremely meticulous, converting all outputs into a common unit,²² taking illness, death and absence as well as workers lent to or borrowed from other overseers into account. The old administrative calendar was still in use – Ur III is the epoch in which sources show that the overseer scribes were to press out of their crew 30 days' work each month irrespective of its actual length. As shown by Robert Englund [35: 46*f* and *passim*], the yearly deficits of an overseer scribe were accumulated, and at his death the family was held responsible for it (if needed by being drawn into the enslaved crews) – at least in private discussion, Englund would speak of the system as a *Kapo* economy.

For use in this immensely expanded accounting, two decisive mathematical innovations appear to have been introduced.

One is the accounting system itself, with built-in automatic controls (in this respect an analogue of what was brought about in the later Middle Ages by the introduction of double-entry bookkeeping). This was taken over in the subsequent “Old Babylonian” period, during which it was also used for private large-scale accounting – after which it was forgotten.

The other was the sexagesimal place-value system. This was a floating-point system, serving equally well for integers and for fractions. It was used for intermediate calculations, of which relatively few traces remain; in mathematical school texts, where orders of magnitude could be presupposed, could be remembered, or were immaterial; and in the late astronomical tables, where the tabular format helped to determine orders of magnitude.

Neither school texts nor astronomical tables can have been the original purpose for which the system was introduced – the latter already for chronological reasons. Nor did it ease additive and subtractive computations

²¹ A survey of the debate about how to interpret the sources on this account is given by Robert Englund [35: 63–68]. The system appears to have been established during what was originally a state of emergency declared at the same occasion as the military reform and which was soon made permanent [35: 57].

²² Often weight of silver, but barley was another possibility – see [35: 18–20].

(which anyhow appear to have been performed on some abacus-like device [36] [37]). What it did facilitate was multiplication and division – but only if multiplication tables and tables of reciprocal numbers were available or learned by heart, along with tables permitting the translation of metrological units into sexagesimal multiples of a standard unit.²³ The production and teaching of such tables, on the other hand, had no point before the place-value system was in use.

This observation leads to a striking conclusion: The important step was not the *invention* of the new notation – which, by the way, was in the air since centuries, as shown by Marvin Powell [33], and may even have been invented well before Ur III without leaving any traces in tablets that happen to have survived and to have been read by Assyriologists. What was decisive will have been a *political decision to implement it* – a decision which could only be effectual in a centralized system like Ur III.

We have no direct evidence for the taking of such a decision nor for where it was taken;²⁴ but we may safely assume that the planning was made in a scribe school environment that was closely connected to the royal administration. Similarly, F. R. Kraus [39: 24-27] concludes that official year names, royal inscriptions and royal hymns were produced in the subsequent Old Babylonian period (see presently) in an institution which at one and the same time served as “palace school” and as “court chancery”, and that this institution went back to some similar Ur III institution.

²³ I borrow the following explanatory example from [38: 18], adapting it slightly:

If a platform had to be built to a certain height and covered by bricks and bitumen, a “metrological table” could be used to transform the different units of length into sexagesimal multiples of the nindan and kūš (“cubit”, $\frac{1}{12}$ of a nindan), allowing the determination of the surface and the volume in the basic units sar [square nindan] and [volume] sar [an area sar provided with a height of one kūš]. A list of “constant coefficients” (igi.gub) would give the amount of earth carried by a worker in a day over a particular distance, the number of bricks to an area or volume unit, and the volume of bitumen needed per area unit – all expressed in basic units (if no transformation into basic units had taken place, different coefficients for the bitumen would have had to be used for small platforms whose dimensions were measured in kūš and for large ones measured in nindan). With these values at hand the number of bricks and the amount of bitumen as well as the number of man-days required for the construction could be found by means of sexagesimal multiplications and divisions – once again facilitated by recourse to tables, this time tables of multiplication and of reciprocal values. Finally, renewed use of metrological tables would allow the calculator to translate the results of the calculations into the units used in technical practice.

²⁴ Until recently, direct evidence for use of the notation during Ur III was itself extremely scarce (and not fully compelling), in particular because of the uncertainty of palaeographic dating of tablets containing only numbers (that is, of mathematical tables and scratch pads for computation). A few years ago, however, Eleanor Robson [personal communication] discovered tables of reciprocals found in dated contexts.

That king Šulgi himself (or at least those who produced propaganda in his name) saw the school as an essential tool for his project is obvious from one of the so-called Šulgi hymns,²⁵ according to which the king was taught from an early age in the “tablet-house”, learning the art of writing together with addition, subtraction, counting and accounting under the protection of the scribal goddess Nisaba; later we hear that his praise is sung in the same tablet house.

Considering the marvellous feats of which Šulgi boasts elsewhere in this and other hymns we may wonder at the level of his mathematical curriculum, far below the actual level of mathematical competence of which the texts of the Old Babylonian age bear witness – even multiplication goes unmentioned, at most it may perhaps be presupposed as an auxiliary technique in accounting (but why then mention addition?). Actually, however, this fits what can be derived from the absence of all mathematical school texts apart from model documents, in particular when viewed in the light of evidence offered by the terminology of the Old Babylonian period. It appears that *problems*, well represented in the (meagre) corpus of mathematical texts surviving from ED III and the Sargonic period, were banished from the Ur III school: it looks as if even the modicum of independent thought needed when students have to find and not just follow a prescribed way was considered a threat to their docility.²⁶

If any ruler ever *was* the state, the deified Šulgi was. The various Šulgi hymns and the prologue of the law-code he produced²⁷ are therefore informative about the official ideology of the state. Šulgi is not only a potent military leader and pitiless avenger of wrongs (which, conveniently, permits him to provide slaves) but also a “good shepherd” and exceedingly just (dual society, passed away in late ED III, had not been resurrected). However, only one feature of his “social justice”²⁸ goes beyond verbatim repetition of the trite commonplaces of the preceding centuries (protection

²⁵ Hymn B, l. 13–19 [40: 31f]. Castellino’s translation and commentary miss the mathematical points.

²⁶ The full argument for this is unfolded in [41].

²⁷ At first ascribed by Assyriologists to his father Ur-Nammu and hence known as the Ur-Nammu laws. The law-code is published with translation in [42: 14–21], hymns B and C in [40], hymns A, D and X in [43].

²⁸ Social justice should be distinguished from “judicial justice”, punishing enforcement of the laws which follow after the prologue.

of orphans from wealthy and widows from mighty men), and only one thus rings true: metrological reform.

All in all, Ur III enhances features which already appeared to characterize proto-literate Uruk: the management of the state was meticulously planned and controlled. This meticulous planning and control had several effects:

- In mathematics, important innovations were introduced – one of them still important for us, given that the sexagesimal place-value system may possibly have provided part of the inspiration for the Indian invention of the decimal place-value system and was certainly the direct inspiration for the introduction of decimal fractions. Free supra-utilitarian developments, on the other hand, appear to have been blocked.
- Socially and ideologically, the fact that the extremely oppressive policies of the system were metered out according to mathematical rules permitted that these policies could be seen by those in power – and probably even by the overseer scribes – as embodiments of *justice*.

The undernourished workers, however, fell ill or ran away the best they could – even this can be read from the accounting texts; after all, they had not been brought up in the scribal school and may have had other opinions about social justice if at all caring about such questions.²⁹ This is likely to be one of the reasons that the Ur III state did not outlast the third millennium. All in all, this early instance of immoderate Taylorism seems to have provoked a reaction similar to what British trade union activist of the twentieth century CE responded to the “scientific management” of their own days: “time and motion studies means that motion stops and time is wasted”.

²⁹ It appears that some of them did. An Old Babylonian epic which seems to reflect Ur III experience and not Old Babylonian conditions (*Atra-hasis*, ed., trans. [44]) transposes a strike into the realm of the gods. After the creation of the world, An takes possession of the heavens, Enlil of the earth, and Enkidu of the waters below the earth – and the minor gods are put to work, digging Euphrates and Tigris. After toiling for forty years they revolt, set fire to their spades and prepare an attack on Enlil’s abode. So much in the account reflects the psychology of real wildcat strikes (Enlil asking who is the instigator, the mutinees answering that everyone is the instigator) that we may safely assume that the story builds on historical experience.

The Old Babylonian period and the culmination of Mesopotamian mathematics

Already around 2025, the periphery rebelled, and the Ur III state lost its character of an empire. A few decades later, even the centre dissolved into small states. Gradually, some of these absorbed the others, and in the eighteenth century BCE Hammurapi of Babylon managed to subdue the whole Mesopotamian south and centre. From then on, this region can be spoken of as “Babylonia”; the centuries from 2000 BCE to 1600 BCE are known as the “Old Babylonian period”; it produced the most sophisticated mathematics we find in ancient Mesopotamia.

This culmination arrived when the mathematical Taylorism of Ur III had disappeared. The period is characterized by individualism, both in the economic structure (even though it would be a mistake to speak of a general market economy) and on the level of ideology or culture [45]. Land, even when owned by the Crown, was often rented under contract. Private correspondence turns up (a large number of letters are published with translation in [46]). The letters were often written by free lance scribes (a category we do not know from Ur III). The Ur III accounting system was now used in private business, handled by privately employed scribes. The seal, so far a symbol of office, now belonged to the individual. We may speak of the rise of an ideology of *personal identity*.

This ideology also affected scribal culture, in a way which is reflected in the texts used in school to inculcate understanding of what should characterize a *real* scribe (the so-called “examination texts” – cf. [47] [48] [49]).

The Sumerian language was dead by now, and Babylonian could be written adequately with a phonetic syllabary of 70 signs or less; a *true* scribe, however, would also use a large number of word signs, borrowed from the Sumerian script but now meant to be pronounced in Babylonian. This, however, was not a sufficient demonstration that the scribe was somebody special. He should also be able to read, write *and speak* Sumerian – a feat only other scribes would be able to appreciate.³⁰ He should know every-

³⁰ A real feat: Sumerian and Babylonian are as different as, for instance, Basque and Spanish. Quite apart from the vocabulary, the scribes should thus understand a grammar based on principles totally different from those of their mother tongue. Without the lexical lists and explanations prepared by the Babylonian masters for their students, nineteenth-century scholars would have been unable to decipher the Sumerian texts.

thing about bilingual texts, he should be familiar with all the significations of the cuneiform signs (each single sign would have one or several phonetic and one or several logographic meanings – to which comes further occult meanings which we do not understand). He should know about music, and about mathematics. The whole complex was called “humanism” (true! – namely *nam-lú-ulu*, Sumerian for “the condition of being human”). Quite adequately, *lú* corresponding to Latin *vir*, another literal but still adequate translation would be “virtuosity”.

The texts from which we know this do not specify *which* kind of mathematics would count as “humanist”. Training tablets which carry a Sumerian proverb on the obverse often have quite simple calculations on the reverse. Elementary mathematics was thus taught at a rather advanced level, and most scribes presumably never went further. On the other hand, however, very sophisticated supra-utilitarian mathematics was also produced, and it is a fair guess that this (as useless as spoken Sumerian) was the really “humanist” level of mathematics.

What we find together with Sumerian proverbs are simple numerical multiplications, area determinations and such things. Before that, future scribes copied metrological tables and tables of reciprocals and multiplication – probably so often that they learned them by heart. All of this was useful training for future professional practice, and hence not supra-utilitarian.

At the sophisticated, supra-utilitarian level we still find numerical problems – for instance, an intricate technique for finding reciprocals of numbers not listed in the standard table nor easily derived from it by successive halving and doubling. The favourite genre, however, was what has been interpreted as “algebra” of the second (at times the third) degree. Nominally, these “algebraic” problems deal with areas of rectangles or volumes of excavations and their sides, at times combined for instance with the wage to be paid for the excavation; the substance of the problems, however, is entirely artificial, and the “algebraic” technique that is taught is completely useless for professional practice. This “algebra” is thus truly supra-utilitarian.³¹

³¹ Not only the terminology but also the technique of the “algebra” in question is geometric – see my [38].

Its inspiration had probably come from a riddle tradition carried by “lay”, that is, non-scribal (whence fully or almost illiterate), Akkadian-speaking surveyors [50]. These riddles (as they can be reconstructed from consideration also of their appearance in much later surveying texts) were of this kind:

“I have added together the side of a square and its area, and the outcome was 110”.

“I have added together the four sides of a square and its area, and the outcome was 140”.

“I have added together the length and the width of a rectangle, and the outcome was 14, while its area is 48”.

“the diagonal of a rectangle is 10, and its area is 48”.

“I have added together the perimeter, the diameter, and the area of a circle, and the outcome was 115”.

Others probably concerned differences between square area and one or all four sides, the sum of or difference between areas and sides of two squares. The total number of the riddles will not have exceeded ten to fifteen.

As mentioned above, mathematical *problems*, and *a fortiori* supra-utilitarian problems, appear to have been totally absent from the Ur III school. As the Old Babylonian scribe school developed, its “humanist” pretensions appear to have induced it to adopt these riddles; in the context of the school, however, a handful of standard riddles could not do: the riddles became the starting point for a genuine mathematical discipline, with rich variation and exploration of the possibilities offered by the technique – for instance, letting the sides of a rectangle represent a number or a price, or even a square area or the volume of a cube (the latter in a problem of the eighth degree, resolvable as a bi-biquadratic). Rich variation had the added advantage of allowing copious training of sexagesimal arithmetic.

Beyond their “humanism”, scribes were (supposed to be) proud, if not of being leading officials of the state (few of them of course were), then of belonging to a group from which leading officials came. This state was still supposed to represent social justice, and serving it could hence be a reason for pride. That can be seen in one of the texts used to form the self-image of scribes in the Old Babylonian school, known as “Lipit-štar, King of

Justice, Wisdom and learning”.³² The king was taught the scribal art by Nisaba, the goddess of scribal wisdom – consisting, the text reveals, in writing and use of “the measuring rod, the gleaming surveyor’s line”, and she bestowed upon him “the cubit ruler which gives wisdom”. The praise goes on

[...] you are Enlil’s son;
 Truth and justice you make manifest;
 Lord, your goodness covers even the horizon.
 King Lipit-eštar, councillor of great judgment,
 (Whose) word never falters, wise one (whose) decision provides justice for
 the people;
 Great mind, knowing all things deeply,
 In order to lay down the law for all foreign countries [...
 ...] you rage against the enemies,
 From evil and oppression you know how to save people
 From sin and destruction you know how to free them.
 The mighty do not perpetrate robbery,
 And the strong do not make the weaker ones into hirelings –
 Thus you established justice in Sumer and Akkad.

The mathematical scribal arts and justice are neighbours, as we see, but the only link beyond this vicinity is indirect, the common reference to generic wisdom.

One step further, the statal social justice of which Hammurapi proclaims himself the supreme protector in the introduction of his famous “law-code”³³ is not mathematical at all but a continuation of commonplaces going back to the outgoing Early Dynastic epoch (Hammurapi is still the protector of orphans and widows); beyond that his justice is judicial (some of his legal decisions, however, concern metrology and punish metrological fraud). One of his successors also issued a decree “re-establishing justice to the country”, prescribing a debt cancellation [53] [54: 151-153], reminiscent of the Old Testament jubilee (Leviticus 25:11-15) but apparently a once-only measure meant to palliate the threat to general econom-

³² Lipit-eštar had been king of Isin, one of the smaller states emerging from the collapse of Ur III. The text was published with translation by H. L. J. Vanstiphout [51].

³³ Text in [42: 76–140]. Actually, the text represents itself not as a law-code but as Hammurapi’s (presumable paradigmatic) judicial verdicts, cf. [52: 228f].

ical stability resulting from a debt crisis and crushing interest rates – in any case a cancellation of the very idea of that “mathematical justice” where everyone receives and contributes his exactly calculated due (indeed the kind of “justice” which had led to the crisis).

Accounting, as mentioned, was still around, but even when done for the state its role was that of a subservient tool. The relation between the state and mathematics had become accidental, not constitutive for either part. Mathematical “humanism” should probably be understood as an *alternative* legitimation rather than as a continuation of the ancient pattern.

Disappearance of a pattern

The final dissolution of the pattern state—social justice—accounting mathematics arrived with the collapse of the Old Babylonian state. After a Hittite conquest of Babylon and ensuing social chaos, power was taken by the Kassite tribes, already present in Babylonia as mercenary soldiers. The ratio between town and countryside dwellers fell to fifth-millennium levels, and the role of scribal administration and culture – always the carriers of ideas of the just state – was not only strongly reduced but also appears (to the extent the extremely meagre written evidence from the period allows us to distinguish) to have lost its ideological hegemony. As writing once again became copious in the late second and the first millennium with the expansion of the Assyrian city-state into a territorial state and finally an empire, we find scribes in central positions at court or somehow working for the court – but now as producers of an ideology emphasizing the king and the empire as creators and upholders of order [55] [56] [57] [58], and as omen priests and astrologers protecting the king [57] [59];³⁴ the huge libraries of the Assyrian royal palaces are also evidence of the activity of learned court librarians and copyists. These

³⁴ The letters from these scholar-scribes collected in [60], apart from giving technical advice, mostly wish the king good health and vigour. One exorcist needing to flatter Assurbanipal – who, in contrast to his predecessors, was pleased to take up themes from earlier epochs – praises him for having brought prosperity to the land (Assurbanipal does boast of that himself, as Hammurapi had done 1100 years before) and for distributing particular favours; the exorcist also states [60: 91] that “the King, my lord, has revived the one who was guilty (and) condemned to death; you have released the one who was imprisoned for many years” (metaphorically, no actual event is meant). Even when trying to appear in the light of age-old traditions, the Assyrian king could only taint Iron-Age despotism with commonplaces of (mainly judicial) justice in Old Babylonian style.

scribes working for or corresponding with the court were certainly also proud of their professional status, but even those of them who may have worked on incipient mathematical astronomy identified themselves as “writers” of omen series, exorcists etc.; mathematics was peripheral to their professional self-esteem.³⁵ Ordinary daily administration was probably taken care of in Aramaic alphabetic writing, and not in cuneiform on clay tablets, for which reason the evidence has disappeared together with traces of the clerks who took care of it.³⁶

To sum up: During the late fourth and the third millennium, “writing” was in power; but “writing” in this respect was first of all accounting and management of resources, somehow connected to the pre-historic redistributive structures. However, during ED III we find the first evidence of literary writing and supra-utilitarian mathematics as evidence of professional self-esteem of scribes, and soon afterwards the use of literature as state propaganda.

During the Old Babylonian period, the role of professional self-esteem becomes much more conspicuous in scribal culture; concomitantly, the legitimization of the state, though still referring to “justice”, is decoupled from accounting.

After the Kassite interlude (the “Babylonian Middle Ages”), “justice” however meant does not characterize the role of the state; activities of importance for professional self-esteem of cuneiform scribes were predominantly literary, divinatory and theurgical.

Bibliography

- [1] Fried, Morton, *The Evolution of Political Society. An Essay in Political Anthropology*. New York: Random House, 1967.
- [2] Service, Elman R., *Origins of the State and Civilization. The Process of Cultural Evolution*. New York: W. W. Norton, 1975.

³⁵ This is no less true in the Seleucid era (third and second century BCE), the epoch where mathematical astronomy attained maturity.

³⁶ Contracts on clay tablets are revealing in this respect. Belonging to a legal genre, they were mostly written in cuneiform Assyrian; but often they carried a resume of some lines in Aramaic – see the specimens in [61].

Some of the contracts, though legal stuff, are in Aramaic, and carry no resume in Assyrian. Contracts on parchment or papyrus, if they existed, will also have been in Aramaic only, the support not being suitable for cuneiform.

- [3] Wright, Henry T., & Gregory A. Johnson, "Population, Exchange, and Early State Formation in Southwestern Iran". *American Anthropologist* 77 (1975), 267-289.
- [4] Schmandt-Besserat, Denise, "An Archaic Recording System and the Origin of Writing". *Syro-Mesopotamian Studies* 1:2 (1977).
- [5] Schmandt-Besserat, Denise, *Before Writing*. I. *From Counting to Cuneiform*. II. *A Catalog of Near Eastern Tokens*. Austin: University of Texas Press, 1992.
- [6] Schmandt-Besserat, Denise, "Tokens as Funerary Offerings". *Vicino Oriente* 7 (1988), 3-9, Tav. I-V.
- [7] Nissen, Hans J., *The Early History of the Ancient Near East*. Chicago & London: University of Chicago Press, 1988.
- [8] Liverani, Mario, *Antico Oriente. Storia, società, economia*. Roma & Bari: Laterza, 1988.
- [9] Nissen, Hans J., Peter Damerow & Robert Englund, *Archaic Bookkeeping: Writing and Techniques of Economic Administration in the Ancient Near East*. Chicago: Chicago University Press, 1993.
- [10] Labat, René, *Manuel d'épigraphie akkadienne (signes, syllabaire, idéogrammes)*. 4^e édition. Paris: Imprimerie Nationale, 1963. ¹1948.
- [11] Baines, John, "The Earliest Egyptian Writing: Development, Context, Purpose". *Max-Planck-Institut für Wissenschaftsgeschichte. Preprint* 180 (2001).
- [12] Damerow, Peter, & Robert K. Englund, "Die Zahlzeichensysteme der Archaischen Texte aus Uruk", Kapitel 3 (pp. 117-166) in M. W. Green & Hans J. Nissen, *Zeichenliste der Archaischen Texte aus Uruk*, Band II (ATU 2). Berlin: Gebr. Mann, 1987.
- [13] Powell, Marvin A., Jr., "Sumerian Area Measures and the Alleged Decimal Substratum". *Zeitschrift für Assyriologie und Vorderasiatische Archäologie* 62 (1972-73), 165-221.
- [14] Aurenche, Olivier, *La maison orientale: L'Architecture du Proche Orient ancien des origines au milieu du quatrième millénaire*. Paris: Paul Geuthner, 1981.
- [15] Beale, T. W., & S. M. Carter, "On the Track of the Yahya Large Kuš: Evidence for Architectural Planning in the Period IVC Complex at Tepe Yahya". *Paléorient* 9:1 (1983), 81-88.
- [16] Englund, Robert K., "Administrative Timekeeping in Ancient Mesopotamia". *Journal of the Economic and Social History of the Orient* 31 (1988), 121-185.
- [17] Luria, Aleksandr R., *Cognitive Development. Its Cultural and Social Foundations*. Edited by Michael Cole. Cambridge, Mass., & London: Harvard University Press, 1976. 1st ed. Moskva: Nauka, 1974.
- [18] Larsen, Mogens Trolle, "The Mesopotamian Lukewarm Mind. Reflections on Science, Divination and Literacy", pp. 203-225 in F. Rochberg-Halton (ed.), *Language, Literature, and History: Philological and Historical Studies presented to Erica Reiner*. (American Oriental Series, vol. 67). New Haven, Connecticut: American Oriental Society, 1987.
- [19] Høyrup, Jens, "Algebra and Naive Geometry. An Investigation of Some Basic Aspects of Old Babylonian Mathematical Thought". *Altorientalische Forschungen* 17 (1990), 27-69, 262-354.

- [20] Høyrup, Jens, "Embedding: Multi-purpose Device for Understanding Mathematics and Its Development, or Empty Generalization?" *Filosofi og Videnskabsteori på Roskilde Universitetscenter*. 3. Række: *Preprints og Reprints* 2000 Nr. 8.
- [21] Kästner, Erich, *Bei Durchsicht meiner Bücher*. Zürich: Atrium Verlag, 1946.
- [22] Carneiro, Robert L., "The Chieftdom: Precursor of the State", pp. 37-79 in G. D. Jones & R. R. Kautz 1981.
- [23] Clagett, Marshall, *Ancient Egyptian Science. A Source Book*. Volume I: *Knowledge and Order*. 2 tomes. (Memoirs of the American Philosophical Society, 184 A+B). Philadelphia: American Philosophical Society, 1989.
- [24] Høyrup, Jens, "Sumerian: The Descendant of a Proto-Historical Creole? An Alternative Approach to the 'Sumerian Problem'". *AIQN. Annali del Dipartimento di Studi del Mondo Classico e del Mediterraneo Antico. Sezione linguistica. Istituto Universitario Orientale, Napoli* **14** (1992; publ. 1994), 21-72, Figs. 1-3.
- [25] Mühlhäusler, Peter, *Pidgin and Creole Linguistics*. (Language in Society, 11). Oxford & New York: Blackwell.
- [26] Romaine, Suzanne, *Pidgin and Creole Languages*. London & New York: Longman, 1988.
- [27] Baines, John, "Literacy, Social Organization, and the Archaeological Record: The Case of Early Egypt", in Gledhill, Bender & Larsen (eds) 1988: 192-214.
- [28] Visicato, Giuseppe, *The Power and the Writing. The Early Scribes of Mesopotamia*. Bethesda, Maryland: CDL Press, 2000.
- [29] Deimel, Anton, *Die Inschriften von Fara. II, Schultexte aus Fara*, in Umschrift herausgegeben und bearbeitet (Wissenschaftliche Veröffentlichungen der Deutschen Orient-Gesellschaft, 43). Leipzig: J.C. Hinrichs'sche Buchhandlung, 1923.
- [30] Visicato, Giuseppe, *The Bureaucracy of Šuruppak. Administrative Centres, Central Offices, Intermediate Structures and Hierarchies in the Economic Documentation of Fara*. (Abhandlungen zur Literatur Alt-Syrien-Palästinas und Mesopotamien, 10). Münster: Ugarit-Verlag, 1995.
- [31] Hallo, William W., "Toward a History of Sumerian Literature", in *Sumerological Studies ...* 1976: 181-203.
- [32] Foster, Benjamin R., "Archives and Record-Keeping in Sargonic Mesopotamia". *Zeitschrift für Assyriologie und Vorderasiatische Archäologie* **72** (1982), 1-27.
- [33] Powell, Marvin A., "The Antecedents of Old Babylonian Place Notation and the Early History of Babylonian Mathematics". *Historia Mathematica* **3** (1976), 417-439.
- [34] Edzard, Dietz Otto, *Gudea and His Dynasty*. Toronto: Toronto University Press, 1997.
- [35] Englund, Robert, *Organisation und Verwaltung der Ur III-Fischerei*. (Berliner Beiträge zum Vorderen Orient, 10). Berlin: Dietrich Reimer, 1990.
- [36] Høyrup, Jens, "A Note on Old Babylonian Computational Techniques". *Historia Mathematica* **29** (2002), 193-198.
- [37] Proust, Christine, "La multiplication babylonienne: la part non écrite du calcul". *Revue d'Histoire des Mathématiques* **6** (2000), 293-303.

- [38] Høyrup, Jens, *Lengths, Widths, Surfaces: A Portrait of Old Babylonian Algebra and Its Kin*. (Studies and Sources in the History of Mathematics and Physical Sciences). New York: Springer, 2002.
- [39] Kraus, F. R., *Vom mesopotamischen Menschen der altbabylonischen Zeit und seiner Welt*. (Mededelingen der Koninklijke Nederlandse Akademie van Wetenschappen, Afd. Letterkunde. Nieuwe Reeks – Deel 36 – No. 6). Amsterdam & London: North-Holland, 1973.
- [40] Castellino, G. R., *Two Šulgi Hymns (BC)*. (Studi semitici, 42). Roma: Istituto di studi del Vicino Oriente, 1972.
- [41] Høyrup, Jens, “How to Educate a Kapo, or, Reflections on the Absence of a Culture of Mathematical Problems in Ur III”, pp. 121-145 in John M. Steele & Annette Imhausen (eds), *Under One Sky. Astronomy and Mathematics in the Ancient Near East*. (Alter Orient und Altes Testament, 297). Münster: Ugarit-Verlag, 2002.
- [42] Roth, Martha, *Law Collections from Mesopotamia and Asia Minor*. Atlanta, Georgia: Scholars Press, 1995.
- [43] Klein, Jacob, *Three Šulgi Hymns. Sumerian Hymns Glorifying King Šulgi of Ur*. Ramat-Gan, Israel: Bar-Ilan University Press, 1981.
- [44] Lambert, W. G., & A. R. Millard, *Atra-hasīs: The Babylonian Story of the Flood*. Oxford: Oxford University Press, 1969.
- [45] Klengel, Horst, “Zur Rolle der Persönlichkeit in der altbabylonischen Gesellschaft”, pp. 109-117 in *Humanismus und Menschenbild im Orient und in der Antike*. Konferenzvorträge, Herausgegeben von der Sektion Orient und Altertumswissenschaften der Martin-Luther-Universität Halle-Wittenberg. (Martin-Luther-Universität Halle-Wittenberg, Wissenschaftliche Beiträge 1977/28 (I 2)). Halle (Saale), 1977.
- [46] Kraus, F. R., *Altbabylonische Briefe in Umschrift und Übersetzung*. 10 vols. Leiden: Brill, 1964-1985.
- [47] Sjöberg, Åke W., “In Praise of the Scribal Art”. *Journal of Cuneiform Studies* **24** (1971-72), 126-129.
- [48] Sjöberg, Åke W., “Der Examenstext A”. *Zeitschrift für Assyriologie und vorderasiatische Archäologie* **64** (1975), 137-176.
- [49] Sjöberg, Åke W., “The Old Babylonian Eduba”, in *Sumerological Studies ... 1976*: 159-179.
- [50] Høyrup, Jens, “On a Collection of Geometrical Riddles and Their Role in the Shaping of Four to Six `Algebras`”. *Science in Context* **14** (2001), 85-131.
- [51] Vanstiphout, H. L. J., 1978. “Lipit-Eštar’s Praise in the Edubba”. *Journal of Cuneiform Studies* **30** (1978), 33-61.
- [52] Renger, Johannes, “Hammurapi’s Stele ‘König der Gerechtigkeit’. Zur Frage von Recht und Gesetz in der altbabylonischen Zeit”. *Die Welt des Orients* **8** (1975/76), 228-235.
- [53] Bottéro, Jean, “Désordre économique et annulation des dettes en Mésopotamie à l’époque paléo-babylonienne”. *Journal of the Economic and Social History of the Orient* **4** (1961), 113-164.

- [54] Edzard, Dietz Otto, “‘Soziale Reformen’ im Zweistromland bis nach 1600 v. Chr.: Realität oder literarischer Topos?” *Acta Antiqua Academiae Scientiarum Hungaricae* 22 (1974), 145-156.
- [55] Liverani, Mario, “The Ideology of the Assyrian Empire”, pp. 297-317 in Mogens Trolle Larsen (ed.), *Power and Propaganda. A Symposium on Ancient Empires*. (Mesopotamia, 7). København: Akademisk Forlag, 1979.
- [56] Garelli, Paul, “L’État et la légitimité royale sous l’empire assyrien” pp. 319-328 in Mogens Trolle Larsen (ed.), *Power and Propaganda. A Symposium on Ancient Empires*. (Mesopotamia, 7). København: Akademisk Forlag, 1979.
- [57] Reade, Julian, “Ideology and Propaganda in Assyrian Art”, pp. 329-343 in Mogens Trolle Larsen (ed.), *Power and Propaganda. A Symposium on Ancient Empires*. (Mesopotamia, 7). København: Akademisk Forlag, 1979.
- [58] Parpola, Simo, “Sons of God – the ideology of Assyrian Kingship”. *Archaeology Odissey Archives*, December 1999.
- [59] Koch-Westenholz, Ulla, *Mesopotamian Astrology: an Introduction to Babylonian and Assyrian Celestial Divination*. (CNI Publications, 19). København: Carsten Niebuhr Institute of Near Eastern Studies/Museum Tusculanum, 1995.
- [60] Parpola, Simo, *Letters from Assyrian Scholars to the Kings Esarhaddon and Assurbanipal*. 2 vols. (Alter Orient und Altes Testament, 5/1-2) Neukirchen-Vluyn: Butzon & Bercher Kevelaer, 1970, 1971.
- [61] Fales, Federico Mario, *Aramaic Epigraphs on Clay Tablets of the Neo-Assyrian Period*. (Studi Semitici, NS 2). Roma: Università degli Studi “La Sapienza”, 1986.

Baroque Mind-set and New Science

A Dialectic of Seventeenth-Century High Culture

Jens Høyrup

Sarton Chair Lecture

13 November 2008

Abstract

The “New Science” of Galileo, Kepler, Harvey, Descartes, Boyle, Steno, etc., and the Baroque in visual arts and literature, are two conspicuous aspects of seventeenth-century European elite culture. If standard historiography of science can be relied upon, the former of the two was not affected by the latter.

The lecture asks whether this is a “fact of history” or an artefact of historiography. A delimitation of the “Baroque” going beyond the commonplaces of overloading and contortion concentrates on the acceptance of ambiguity and the appurtenance to a “representative public sphere”, contrasting with the quest for clarity and the argument-based public sphere of the new science, suggesting that Baroque and New Science were indeed incompatible currents. A close-up looks at Juan Caramuel y Lobkowitz, who was a major Baroque theoretician but also wrote much on mathematics, finding even within his mathematics love for ambiguity. The way his mathematics is spoken about in the Oldenburg correspondence shows that the mainstream of the New Science saw no interest in this.

The watershed

Modern science – this is generally agreed upon – was inaugurated in the seventeenth century by characters such as Galileo, Kepler, Harvey, Descartes, Pascal, Huygens, Boyle, Hooke, Steno and Newton. There is

also broad consensus that conspicuous sixteenth-century figures like Copernicus, Tycho, Cardano, Vesalius and Bombelli (not to speak of Dee, della Porta and Paracelsus) opened the way for the breakthrough by carrying the ancient and medieval inheritance beyond the bursting point; but that they left synthesis to a future generation.

Retrospectively, Galileo etc. count as belonging within natural science – the domain which in English in more recent times became *science simpliciter*. However, we do not need to restrict our argument to this domain. The natural law doctrines of Locke and Pufendorf, Hobbes’s political theory based on a non-Aristotelian concept of nature, and the *Grammaire générale* of Arnauld and Lancelot are also modern, while (say) Machiavelli forebodes modern political thinking in a way which makes his ancient models crack but does not yet reconstruct.

It is customary to categorize Paracelsus, Copernicus, Vesalius, Cardano, Dee, Brahe, Bombelli and della Porta as “Renaissance scientists”, and it is indeed not difficult to point to features of their thought that are widespread within the Renaissance movement. In contrast, there is no tradition for seeing Galileo, Kepler, Harvey, Descartes, Pascal, Huygens, Boyle, Hooke, Steno, Newton, Hobbes, Locke, Pufendorf and Arnauld as exponents of the Baroque, the indubitable general cultural importance of the Baroque for their century notwithstanding.¹

One may ask – and that is what I am going to do – whether this is a historical or a historiographical conundrum. In other words: is it true that the New Science (or “new philosophy” as it was rather called at the time) and the Baroque represent contemporary but unconnected or perhaps even conflicting cultural currents? Or, have historians of science simply been blind to the relation between the two? Is the Baroque a context without (scientific) texts, or is it simply so much in disrepute among historians of science that they do not wish to associate it with their heroes?

¹ The recent “Baroque Science” project of Sydney University should be mentioned as an exception – see <http://www.usyd.edu.au/baroquescience>. It formulates the contrast in these terms:

‘Baroque’ refers to the preoccupation with paradox and contrast, with asymmetry and distortion, with imagery and sensual detail. ‘Science’ is the search for simple, universal structures, eschewing rhetorical embellishment for logical rigor and sense qualities for the austerity of matter in motion

which then allows the project to allow harmony between the two by looking *differently* at seventeenth-century science.

The question dawned to me during teaching of the history of the humanities. First I wondered that the Spanish *siglo de oro*, in spite of its importance in the general cultural landscape, seemed not to have left traces calling for the attention of historians of science; then I got the idea that at least the “etymological current” in linguistics might have to be understood within the Baroque framework. In Sweden and Denmark this current is best known through Olaus Rudbeck’s *Atlantica* [1] – famous in Sweden, notorious in Denmark: charming in Sweden and shocking in Denmark, indeed, the idea that precisely *Swedish* should be the language of Paradise! My starting point was thus not too far removed from that of Gunnar Eriksson’s in *The Atlantic Vision: Olaus Rudbeck and Baroque Science* [2].

Delimitation of the Baroque

This starting point was a mere intuition, and it is not strange that Eriksson and I took different directions when leaving it, Eriksson making a complete portrait of Rudbeck’s science, I myself returning to the initial question about the relation between the Baroque and the New Science.² In order to make this return fruitful we have to go beyond the everyday understanding of the Baroque as mere “baroque”, as mere contrast to the classicist ideal of *edle Einfalt und stille Größe*. Is it possible to define the Baroque, to delimit it, or at least to characterize it?

A first strategy is the chronological approach. It is familiar from the commonsense historiography of music, where everything between Monteverdi and Bach is “baroque music” simply because of its date. This approach is that of Reijer Hooykaas and J. E. Hofmann, among the few historians of science who do mention the Baroque. Hooykaas [5: 161] speaks of modern science as produced by “scientists of the Renaissance and Baroque periods”, whereas Hofmann’s ultra-concise *Geschichte der Mathematik* [6] has the chapter headings “Übergang zum Barock (1450-1580)” (vol. I, p. 100), “Frühbarock (etwa 1550 bis 1650 n. Chr.)” (vol. I, p. 116), “Hochbarock (etwa 1625 bis 1665)” (vol. II, p. 4) and “Spätbarock (etwa 1665 bis 1730)” (vol. II, p. 50).

² My earlier work on the topic is contained in [3] and [4].

With this definition, everything is easy. Arnauld is neither more nor less Baroque than Rudbeck. The problem is neither historical nor historiographical but linguistic: the concept is empty, and we may calmly leave it to Occam's razor to dispose of it.

However, according to the same line of thought, Racine is neither more nor less Baroque than Calderón. If we insist that there *is* a difference and do not accept this elimination of the concept of the Baroque from the history of art and literature, then our problem returns. If the Baroque exists as a *particular* current of seventeenth-century elite culture within which Calderón belongs but to which Racine is in opposition, then it is still legitimate and meaningful to ask whether *this* particular current imprinted the New Science of the seventeenth century.

This approach corresponds to René Wellek's reflections on "Baroque in Literature" [7]:

The term baroque seems [...] most acceptable if we have in mind a general European movement whose conventions and literary style can be fixed narrowly, as from the last decades of the sixteenth century to the middle of the eighteenth century in a few countries.

Obviously, a "current" or "movement" cannot be strictly defined. Even a delimitation – the original meaning of the word we translate as "definition" in Euclid's *Elements* – cannot be exact. Yet we may strive to dig out central characteristics, features which distinguish the core of the current but only in weakened form or not all together when we look at its periphery.

In its origin, the Baroque is linked to the Counter-Reformation and the Jesuit order – the latter to such an extent that *Il grande dizionario Garzanti* [8] explains "stile gesuitico" as "il barocco, in architettura e in letteratura".³ In 1563, the Council of Trent issued a decree stating among many other things that ecclesiastical art was to serve the propagation and consolidation of orthodox faith.⁴

And if any abuses have crept in amongst these holy and salutary observances, the holy Synod ardently desires that they be utterly abolished; in such wise that no images, (suggestive) of false doctrine, and furnishing

³ See for instance Arnold Hauser's [9: 69–72] and Rudolf Wittkower's [10] discussions.

⁴ Translation from [11: 235f].

occasion of dangerous error to the uneducated, be set up. And if at times, when expedient for the unlettered people; it happen that the facts and narratives of sacred Scripture are portrayed and represented; the people shall be taught, that not thereby is the Divinity represented, as though it could be seen by the eyes of the body, or be portrayed by colours or figures.

Moreover, in the invocation of saints, the veneration of relics, and the sacred use of images, every superstition shall be removed, all filthy lucre be abolished; finally, all lasciviousness be avoided; in such wise that figures shall not be painted or adorned with a beauty exciting to lust [...].

In fine, let so great care and diligence be used herein by bishops, as that there be nothing seen that is disorderly, or that is unbecomingly or confusedly arranged, nothing that is profane, nothing indecorous, seeing that holiness becometh the house of God.

And that these things may be the more faithfully observed, the holy Synod ordains, that no one be allowed to place, or cause to be placed, any unusual image, in any place, or church, howsoever exempted, except that image have been approved of by the bishop”.

That could not and did not determine how and what art should *be*, at most what it should *not* be – the loincloth painted over Michelangelo’s naked Christ in the Sistine Chapel is an almost parodic example.

In so far, the emergence of the Baroque can be seen in the perspective of an observation made by Carlo Ginzburg [12: 146, my translation], regarding

a problem the significance of which is only now beginning to be recognized: that of the popular roots of a considerable part of high European culture, both medieval and postmedieval. Such figures as Rabelais and Brueghel probably weren’t unusual exceptions. At the same time, they closed an era characterized by hidden but fruitful exchanges, moving in both directions between high and popular cultures. The subsequent period was marked, instead, by an increasingly rigid distinction between the culture of the dominant classes and artisan and peasant cultures, as well as by the indoctrination of the masses from above. We can place the break between these two periods in the second half of the sixteenth century, basically coinciding with the intensification of social differentiation under the impulse of the price revolution. But the decisive crisis had occurred a few

decades before, with the Peasants' War and the reign of the Anabaptists in Münster. At that time, while maintaining and even emphasizing the distance between the classes, the necessity of reconquering, ideologically as well as physically, the masses threatening to break loose from every sort of control from above was dramatically brought home to the dominant classes.

This renewed effort to achieve hegemony took various forms in different parts of Europe, but the evangelization of the countryside by the Jesuits and the capillary religious organization based on the family, achieved by the Protestant churches, can be traced to a single current. In terms of repression, the intensification of witchcraft trials and the rigid control of such marginal groups as vagabonds and gypsies corresponded to it.

However, the implementation of the Trent programme was made, and could hardly avoid to be made, on the foundation of existing art, that is, the Mannerist trend, and (since Jesuits were main responsible) with strong regard for Ignazio de Loyola's insight in the importance of the active emotional involvement of the recipient: as explained in §2 of his *Ejercicios espirituales*, the religious message must never be so explicit and direct that the spiritual commitment of the recipient is barred.⁵

[...] if the person who is making the contemplation, takes the true groundwork of the narrative, and, discussing and considering for himself, finds something which makes the events a little clearer or brings them a little more home to him [...] he will get more spiritual relish and fruit, than if he who is giving the Exercises had much explained and amplified the meaning of the events. For it is not knowing much, but realizing and relishing things interiorly, that contents and satisfies the soul.

This advice not to tell too explicitly is already in potential conflict with the Trent request that "the people shall be taught, that not [by religious images] is the Divinity represented, as though it could be seen by the eyes of the body, or be portrayed by colours or figures".

The essential point in Loyola's method is not presentation of the religious motif by itself but the motif embedded in a totality of tension, colour and

⁵ I follow Elder Mullan's translation [13], after collating with the edition in [14: 11].

movement. Loyola prescribes thus how to get an “interior sense of the pain which the condemned suffer” (§§65-70, after [13], cf. [14: 27f]):

The first Point will be to see with the sight of the imagination the great fires, and the souls as in bodies of fire. The second, to hear with the ears wailings, howlings, cries, blasphemies against Christ our Lord and against all His Saints. The third, to smell with the smell smoke, sulphur, dregs and putrid things. The fourth, to taste with the taste bitter things, like tears, sadness and the worm of conscience. The fifth, to touch with the touch; that is to say, how the fires touch and burn the souls.

Transferring this principle to the realm of art, Gabriele Paleotti, cardinal and bishop of Bologna, declares in his *Discorso intorno alle imagini sacre e profane* (I, xxv, from 1594; my translation from [9: 71f]):

Telling the martyrdom of a saint, the zeal and constancy of a virgin, the passion of Christ himself, are things that touch the true; but when they are present in live colours, here in front of the eyes the martyred saint, there the virgin assaulted, and on the other side the nailed Christ, this truly increases the devotion and wrings the bowels, so that he who does not feel it is made of timber or marble.

This reveals another aspect of the Baroque: the Baroque work of art is a *Gesamtkunstwerk*, a planned totality where all elements are to fit together – in good agreement also with the connection between the Baroque and court culture. In the terminology of the young Habermas, the Baroque is a “representative public sphere” (*Repräsentative Öffentlichkeit*), the exhibition of “truth” *ad oculos*, beyond possible doubt or debate (though certainly not beyond idiosyncratic personal interpretation).

A strong emotional involvement of the flock impedes criticism and rational doubt and is thus fundamental for the functioning of a representative public sphere; but the clerical insight in its necessity prevented the degeneration of art into one-dimensional didactic, however much the bishops from Trent had aimed at exactly that. The Jesuit Antonio Possevino (1534-1611), friend of Clavius, thus writes in his *Tractatio de Poësi et Pictura ethnica, humana et fabulosa collata cum vera, honesta et sacra* (1595)⁶ that

⁶ Translated after Paola Barocchi's edition [15: II, 458].

the painter should take advantage of the whole of philosophy, in particular of moral philosophy, since the depiction of the soul and the expression of all its sentiments, agitations and other commotions makes the art of painting deserve the highest praise. The soul, indeed, being various, irascible, just, inconstant, and abominable, clement, sweet, compassionate, sublime, vain-glorious, humble, proud, and frivolous, he who is able to do that is certainly not lacking in acuteness of mind.

These quotations allow several supplementary observations touching at our topic.

Firstly, we may return to the quotation from Ginzburg and take note of the contrast between Possevino's outlook (which he shared with many Jesuits and with much Jesuit practice) and the one-way moralizing of Puritanism and Lutheran orthodoxy: none of these could accept a similar inextricable conglomerate of good and evil. It may be no accident that witch burning was less common in regions where Jesuit Baroque culture was strong than in Lutheran areas (although, as has been observed, the Spanish inquisition may simply have been too busy burning heretics to bother much about witches).

Secondly, we may notice that erudite Baroque poetry – say, that of Góngora, Donne and Gryphius – is not at all fit to serve “the indoctrination of the masses from above”, and in so far not easily related to the Trent decree and its definition of the tasks of (church) art. This kind of poetry can be understood, however, exactly in the context of the way Paleotti, Possevino and others filled out the programme. We may think of this passage from John Donne [16: 178]:

I throw myself down in my chamber, and I call in and invite God and his angels thither, and when they are there I neglect God and his angels for the noise of a fly, for the rattling of a coach, for the whining of a door. I talk on, in the same posture of praying, eyes lifted up, knees bowed down, as though I prayed to God; and if God or his angels should ask me when I thought last of God in that prayer, I cannot tell. [...] A memory of yesterday's pleasure, a fear of tomorrow's dangers, a straw under my knee, a noise in mine ear, a light in mine eye, an anything, a nothing, a fancy, a chimera in my brain, troubles me in my prayer.

Loyola had also known about such disturbances (*Ejercicios Espirituales* §§346-351 [13] [14: 84f]); but ultimately he ascribed them to “the enemy”. The champion of the Counter-Reformation thus could still provide dichotomic simplicity by means of projection and reification; the Baroque poet, like the theoretician Possevino, had come to acknowledge the inherent quiet disorder of the human mind.

On the other hand, and finally, there is a striking contrast between Possevino’s words and much of what we find with central representatives of the New Science – Bacon’s belief that nature can be reduced to a finite number of forms; Descartes’ clear and self-evident truths;⁷ the certainty of the geometric method; the conviction of Boyle and others that the *experiment* can establish solid facts; the faith of Descartes, Boyle, Leibniz and others that the mechanized thought of algebra may serve as a general model for the scientific and philosophical method.

General explanations

This latter contrast suggests a first general explanation of the absence of Baroque inspiration in the New Science: the two cultural currents have radically different programmes. We may think of Galileo’s vicious remarks about Sarsi alias Orazio Grassi in *Il saggiatore* – the Collegio-Romano mathematician who had dared to suppose a comet to be farther away than the moon (and to point out that Galileo could not have performed his experiments too carefully):⁸

It seems to me that I discern in Sarsi a firm belief that in philosophy it is essential to support oneself on the opinion of some celebrated author, as if when our minds are not wedded to the reasoning of some other person they ought to remain completely barren and sterile. Possibly he thinks that philosophy is a book of fiction created by some man, like the *Iliad* or *Orlando furioso* – books in which the least important thing is whether what is written in them is true.

⁷ We may also observe that Descartes reproduces Loyola’s dichotomy by other means when he separates “the passions of the soul” from the soul itself (which is essentially *thought*).

⁸ Translation from [17: 183].

At first we may believe that Galileo just postulates the incompetence of his opponent – Benjamin Farrington’s words from 1938 [18: 437] come to mind:

There is a phrase that has been much on people’s lips in recent times to the effect that science is ethically neutral. It is, no doubt, possible to attach a meaning to this. But it is also surely true that with regard to one, at least, of the cardinal virtues science is not neutral: Science must be true.

However, certain turns in Galileo’s assault hint at a more precise aim. Firstly, in the treatise which Galileo attacks, Grassi plays with Baroque rhetoric and metaphors, albeit showing that these *are* metaphors by explaining them; secondly, he permits himself to refer to the testimony of ancient philosophers and even to such poets who – like Ovid and Lucrece – were familiar with mathematics and natural philosophy

For one reason as well as the other, Galileo can insinuate an identification of Grassi with *probabilism* [19: 23f], a doctrine according to which “in matters of faith and morality, it suffices for the assurance of tranquillity of conscience to follow a plausible opinion” ([20: A3] – where “plausible”, that is, *probabilis*, means that an opinion is shared by one of several (possibly discordant) recognized authorities. As observed by the horrified Pascal, the consequence is that most humans will be innocent.⁹ That horror may be one of the reasons Pascal and Arnauld created the concept of quantified probability: without quantification, the opposite *probabiliorist* doctrine – that the *most* plausible opinion must be followed – is ultimately meaningless.

Beyond the Baroque acceptance of ambiguity and the tie between Baroque culture and probabilism, we find another global conflict between the Baroque and the New Science as the latter developed in the course of the seventeenth century. As mentioned, the Baroque was a “representative public sphere” – maybe the most striking deliberate construction of this type of public sphere before the advent of modern advertising. In this respect there is no fundamental conflict with the roots of Modern science in courtly culture, as discussed by William Eamon [22]. However, from around 1615 the barycentre moved toward circles of peers, from the meet-

⁹ *Les Provinciales* VI [21: 719].

ings in Mersenne's cell over Gresham College to the creation of the scientific academies (to mention but the emblematic names). Thereby, the ambience of the New Science became an exemplification of the other main type of "public sphere" understood as locus for the creation of collective conviction: the one where "truth" is not displayed but results from discussion based on more or less well-defined shared principles between culturally qualified participants who, with respect to the discussion, are in principle peers¹⁰ – the type of public sphere which the young and still neo-liberalist Habermas believed to have emerged only with (petty) bourgeois society.¹¹ It is characteristic that striking *displays* of the new truth like those of Otto von Guericke were performed for the Emperor and for the Berlin court [28: 168] [29: 575]. More representative than the display of the Magdeburg hemispheres is what Lorenzo Magalotti, secretary of the Accademia del Cimento, wrote about Leopold, Medici prince and protector of the Academy.¹² Leopold liked

to act as an Academician, and not as a Prince. He is content to play the second role only on occasions when there is a question of expense, generously supplying the needs of the Academy.

Close-up

Birds eye views are useful. The contrast between the quest for simplicity and clear-cut answers on one hand and the acceptance of and even infatuation with ambiguity on the other is probably a valid contribution to our understanding of why a Baroque influence on the New Science is difficult to discern; the reference to the foundation of the two currents in public

¹⁰ This point could evidently be elaborated and modulated. On one hand, the integration of the *Académie des Sciences* in Colbert's state system had as one consequence the introduction of a hierarchy of *pensionnaires*, *associés* and *élèves*; on the other, printing gave new opportunities for the development of a *republic of letters* encompassing all of those who had received adequate education (in whatever way they had received it). Indeed, the norm that knowledge should be made public (as knowledge that can be *understood*) is already expressed in the sixteenth century in as unanticipated places as John Dee's *Monas hieroglyphica* from 1564 [23] and della Porta's *Magia naturalis* from 1591 [24], cf. [25: 349f, 342f – cf. also Pamela Long's discussion [26] of the norm of openness as expressed in sixteenth-century writings on mining and metallurgy]. Since this is not my present theme, I shall restrict myself to these hints.

¹¹ This expansion of Habermas' conceptual framework is presented in Danish in my [27], together with a discussion of pre-bourgeois instances of an "argument-based public sphere".

¹² Quoted from [30: 56f]. Even though the claim may not be fully true (it seems not to be) it illustrates the ideal with which the secretary found it fitting to measure him as an academy member.

spheres of discordant types is also likely to make a cogent point. However, it may be useful to look at these general explanations through the lens of a particular example: a character who was deeply rooted in the Baroque mind-set and at the same time participated in the unfolding of the New Science, or at least tried to do so – at best participating in its mathematical and natural-science main current.

Two formidable characters propose themselves. One is Athanasius Kircher, the other is Juan Caramuel. Kircher's activity ranges more widely in the natural-scientific field than Caramuel's; Caramuel, on the other hand, is more explicit as a theoretician of the Baroque. I shall concentrate on Caramuel, returning briefly to Kircher, and mention Rudbeck in an aside.

Even though all three are polymaths, we should not necessarily take all polymathy as a characteristic Baroque value: much of it, for instance Alsted's encyclopaediae, comes in the wake of Ramism, which in its love for dichotomic simplicity is at least as far removed from the Baroque as the New Science.

Caramuel's Baroque

Caramuel was born in Madrid in 1606. He studied theology and entered the Cistercian Order at an early age, and died in 1682 after having been bishop, first of Campania¹³ and afterwards of Vigevano close to Milan. Many among his more than 70 volumes can be linked to the theory of the Baroque.

One of them is his *Defence of the age-old and universal doctrine, about probabilism. Against D. Prospero Fagnani's new, singular and implausible opinion* [20]. The above maxim used to explain "probabilism" was borrowed from the introductory résumé of this work. Further on in the same résumé Caramuel states (exactly one hundred years after the Trent council!) that

¹³ Thus in that same depressing area which Christ never reached because he "stopped at Eboli", as Carlo Levi's local interlocutors claimed. For Caramuel no less than Levi, writing was a way to survive mentally.

if the theologians will be allowed for another hundred years to constrain consciences with the same force as they have done these last hundred years, then the conversion of the infidels will be made very difficult, and also for the orthodox very great difficulties will most certainly have to be feared.¹⁴

No wonder that Pascal, convinced of the sinfulness of all men, protests time and again against Caramuel's tolerance in his *Lettres provinciales* (cf. note 9).

Already in 1635 Caramuel had published an *Easy and Clear Explanation of Steganography, or of the Key of the German Solomon, Ioannes Trithemius* [31]. Since Trithemius had introduced it in the early sixteenth century, "steganography" (the art of concealed writing) was in odour of cabbala and black magic (for which reason Trithemius's book was only printed a hundred years later; cf. [32] [33: 169]); Caramuel exonerated it of all dependency on demonic pact or superstition, understanding the cryptographic technique instead as a way to uncover the secrets of the mind through connotations.¹⁵

Caramuel's *Metametrical* from 1663 [35] is an extensive treatment of poetical techniques. Here (p. 1 of the treatise "Apollo analexicus") he phrases the programme that

The whole machine of the world is full of Proteus. Wherefore let us grasp a Proteic pen, that we may be able to praise Proteus

and he praises ("Apollo logogriphicus" p. 215) the logogriph as an

enigmatic song, which digs many significations from the same name, reading backwards, taking away letters or adding others.

If anybody, Caramuel is thus an exponent for Baroque ambiguity, for the use of connotative appeals rather than explicit messages. The word "audacious" (*audax*) recurs in several of his titles – a *Grammatica audax* is the

¹⁴ *Demonstratur tandem Theologos, ita centum annis ultimis constrinxisse Conscientias, ut si aliis centum eodem impetu pergere permittantur, reddetur difficillissima Infidelium conversio, et apud ipsos Orthodoxos inconvenientia maxima certissimè timeri poterunt.*

Here and everywhere in the following, translations from Caramuel's Latin are mine.
¹⁵ Actually, in a treatise *Cabala, hoc est, secretior interpretatio Sacrae Paginae* (apparently never published but referred to in the initial unpaginated list of Caramuel's publications in [34]) he did the same to cabala itself, using it to find hidden meanings in the Scripture. In the same place he tells that his *Metametrical* (on which imminently) was nothing but a reinterpretation of cabala, given this new name because of the notoriety of the old one.

“praecursor logicus” to his *Theologia rationalis* (1554-55), and there is even a *Mathesis audax* from 1644.¹⁶ Even Caramuel’s understanding of etymology is, as we shall see, “audacious”: It is not necessarily meant to reveal the true historical origin of words but rather, like the logograph, to reveal concealed possible meanings.¹⁷

Caramuel the mathematician

After 1663, the Jansenists and the Dominican probabiliorists got the better of Caramuel, and he was no longer allowed to persist in moral and theological tolerance. Instead he published two huge volumes in 1670 about one of his other interests, namely mathematics. His *Mathesis biceps* [34], divided into “old mathematics” and “new mathematics”, runs over more than 1800 folio pages.

About this work – the only one he mentions in his short “scientific biography” – Juan Vernet [39] tells that

¹⁶ The full title is nothing less than *Mathesis audax rationalem, naturalem, supernaturalem, divinamque sapientiam arithmetica, geometrica, catoptrica, statica, dioptrica, astronomica, musica, chronica, et architectonica fundamentis substruens exponensque*. I have not been able to see it, but according to the secondary literature it deals with combinatorics (that is, we may observe, the mathematics of the anagram), meant to replace and outdo Aristotle’s *organon* as a universal key to all sciences – see [36: 128] [37: 118] [38: 282–284].

¹⁷ On this point, reading of Caramuel may elucidate Rudbeck’s programme. In *The Atlantic Vision*, Eriksson [2: 134] states that for Rudbeck the etymologies of the *Atlantica* have “a rather small degree of credibility”, because Rudbeck compares them to “ornaments and paintings” on a building, whose walls and roof are constituted by the ancient written sources, whereas Swedish nature itself makes up the fundament. However, the text which Eriksson quotes continues in a way which shows that something different than mere low credibility is at stake (I quote from Eriksson’s translation, repairing an omission):

Ornaments and paintings do not please all in like measure, for as one person wants green the other wants grey, when the one likes Doric the other likes Ionic. With this I mean the style and the origin of words, for maybe one is more pleased if Neptune has his origin from bathe or depict rather than from ruling the sea, and Hercules rather from being the Honour of Juno (the weather) or etc., than from being a warrior chief.

The walls and the roof are what I call the writings of the ancients with which the building is put together. If they do not tell the truth, neither could I. For I did not live in the time of Troy or before.

The foundation is what I call the country of Sweden, its lakes, mountains and streams and other such things through which the ancients have described Sweden’s certain position, all of which features remain undisturbed until the stone, mentioned by Daniel, who himself planted it, falls from heaven crushing everything.

The ancient written sources thus have a lower credibility, compared to the arguments from geographical facts. Etymologies, on the other hand, are a domain which allows audacious subjective choice and where “the least important thing is whether what is written [...] is true”.

although it contains no sensational discovery, [it] presents some original contributions to the field of mathematics. In it is expounded the general principle of the numbering systems of base n (illustrated by the values 2, 3, ..., 10, 12, and 60), pointing out that some of these might be of greater use than the decimal. He also proposed a new approximation (although he did not say so) for trisecting an angle. Caramuel developed a system of logarithms of which the base is 10^9 , the logarithm of 10^{10} is 0, and the logarithm of 1 is 10. Thus, his logarithms are the complements of the Briggsian logarithms to the base 10 and therefore do not have to use negative characteristics in trigonometric calculations. In these particulars Caramuel's logarithms prefigure cologarithms, but he was not understood by his contemporaries; some, such as P. Zaragoza, raised strenuous objections.

This could make us believe that Caramuel's mathematics is as easily separable from his Baroque poetics as Newton's *Principia* from his "chronology of ancient kingdoms" [38]. This, however, turns out to be yet another confirmation of Léon Rodet's principle [41: 205] that "when studying the history of a science, exactly as when one wants to obtain something, one should 'rather ask God himself than his saints'".¹⁸

At first we may look at what Vernet sees as a presentation of "the general principle of the numbering systems of base n ". It turns up as a *meditatio prooemialis* before the treatment of arithmetic (proper), and is an answer to the question (p. xliii)

whether arithmetic be one, or several? If several, which they may be? And how do they differ from each other? Are they practical, or speculative? And are they necessary?

Caramuel's intention is not to produce a "general principle" but exactly the opposite. After having described place value systems with base 2, 3, 4, 5, 6, 7, 8, 9, 10, 12 and 60 (explaining where each may be useful) and shown how to calculate in base 2, 3 and 4 he concludes (p. lxvi; italics from the original) that

Firstly, it is thus established *that several arithmetics are possible, which differ from each other*: indeed, as there are various languages in the world,

¹⁸ "Pour étudier l'histoire d'une science, tout comme pour obtenir quelque chose, 'il vaut mieux avoir affaire au bon Dieu qu'à ses saints'".

so they can be dissimilar, and varied with respect to the first return of the unit. I intend, 2, 3, 4, etc.,¹⁹ as we have shown above.

Secondly, it is established that *all these arithmetics are analogous*: indeed, as all languages agree analogically in their flow, similarly, or certainly even more strictly, the arithmetics agree. [...].

Thirdly, it is established *that before the operation of the mind there is neither number not arithmetic. Truly, numbers are entities produced by the intellect*:²⁰ *and that the return of the same numbers depends on human free will; and that these go back to the beginning at so many, and neither by more nor fewer units is because it pleased those who first fashioned arithmetic thus and not otherwise.* [...].

We may find the level rather elementary, but Caramuel was none the less the first to publish about different place value systems and describe algorithms for calculating with them.²¹ The metamathematical stance is even more original, too original indeed to the taste of mathematicians: only the non-Euclidean geometries of the nineteenth century led some mathematicians to accept this kind of pluralism; most, even then, only accepted the non-Euclidean variants when Felix Klein had reduced even this pluralism to a single “general principle”. It was never the prevalent habit of mathematicians to stress the free subjective choice.

In the *Mathesis biceps*, on the contrary, subjective choice turns up even in places where we would expect Caramuel’s choice to be anything but free. Time and again he returns to the choice between the Copernican, the Tychonic and the Ptolemaic world system, and as we should expect from a Catholic bishop in 1670 he rejects the Copernican option. His formulations, however, are not as we would expect. He does not say that this system is contrary to Sacred Scripture but (p. 1392b) that “the cardinals have declared it to be contrary to Sacred Scripture” (which indeed they had; the statement is preceded by a list of “famous mathematicians” – Galileo,

¹⁹ The meaning is that in the dyadic system, the unit “returns” as 2 (which will be written 10), etc.

²⁰ In the next paragraph, Caramuel emphasizes that numbers are not chimerical figments of the mind but *formed* by the mind, and that *after* the operation of the mind they truly exist in things. His “relativism” is Einsteinian (no frame of reference is privileged, but all are equivalent and translation is possible), not postmodern in Feyerabend-Latour style.

²¹ Harriot had done as much before, but in an unpublished note [42]. In the early thirteenth century, Jordanus de Nemore had explained the possibility of place value *fractions* with different bases, speaking of them as “consimilar fractions”, and confronting with “dissimilar fractions”, ascending continued fractions with changing divisors.

Kepler and others – who support the Copernican system).²² Caramuel's own opinion is stated in phrases like “for me, the earth stands still” (p. 1581a) or (p. 1400b)

We have no need for that which the Church has condemned. When hence the Copernican system has been rejected, the two others remain in court. The Ptolemaic system is implausible [*improbabile*]: Nobody can indeed deny that Venus and Mercury move around the sun. Thus the Tyconic system stands.

Algebra!

Caramuel wrote long after Cardano, Bombelli, Viète and Descartes, and it therefore seems adequate that algebra is treated on 108 folio pages. What is immediately striking is that these pages belong to the first volume, “ancient mathematics”. However, this location turns to be well-founded. Nothing of what these four authors had done has indeed left the least trace in Caramuel's algebra.

This does not mean that Caramuel just explains or repeats what can be found in algebraic writings from the earlier Renaissance or the Middle Ages. As far as I know, *no* precursor ever dealt with the material as does Caramuel. His basic idea – *a free choice* if any – is that algebra or “abstract proportion” is an extension of the “false position” and the rule of three.²³ For this reason, his algebra never goes beyond the first degree, even though his presentation of algebraic symbolic notations suggests a notation for higher powers which in principle is related to that of Bombelli (but so different in its concrete shape that borrowing can be excluded).

²² Elsewhere (p. 105) he declares the stance of the cardinals to be *prudent*, because nothing in the Sacred Scripture suggests the earth to move, but much that it rests.

²³ Both terms may be in need of explanation.

First the “false position”, which may be “simple” or “double”. A number, to which $\frac{1}{7}$ of itself is added, gives 19. In the “simple” variant we make a convenient but probably false guess – for instance, that the number is 7. Adding its $\frac{1}{7}$ gives us 8 – but we should have $\frac{19}{8}$ as much. Therefore, our guess should also be multiplied by $\frac{19}{8}$. In the “double” variant we make two guesses (for instance, 7 and 21), and find the result as a mean, weighed in inverse proportion to the two resulting errors (the principle of alligation).

Next the “rule of three”. 3 sacks of flower cost 17 shillings, what is the price of 4 sacks? The rule, as it is formulated in late medieval abacus books, prescribes that we multiply [the counterpart of] the things we want to find (that is, 4, namely 4 pounds) but the magnitude which is not of the same kind (17, namely shillings) and divide by the third magnitude (3, pounds).

Both methods, we see, are rather *alternatives* to algebra as we know it from the medieval treatises than fundaments for it.

I shall take up only a few aspects of Caramuel's idiosyncratic algebra. At first (pp. 99-110) comes a philosophical deliberation whether it is possible to derive true conclusions with necessity from false premises. This deliberation is necessary precisely because of the identification of algebra with the "false position". Caramuel rambles widely. He moves through the schemes of Aristotelian logic (not least of course *modus tollens*, the "indirect proof" whose schematic figure called *barocco* may indeed have given rise to the nickname which the Enlightenment gave to seventeenth-century art²⁴); the fictions of legal thought; *theorica planetarum* with its falsely assumed epicycles and crystal spheres; logarithms; the indirect proofs of mathematics; and finally the false position. The conclusion is a denial of the possibility – Caramuel, like Farrington, thinks that "science must be true", his steganography and logogriphs should not be seen as a rejection of the demand for truth; but as Paleotti's way towards piety, the path toward truth may be indirect, poetical rather than through explicitly argued discourse.

This is clearly exemplified in what follows on pp. 117-119: an etymological investigation of the origin of the names of algebra: *algebra*, *cozza* and *almucabala*.

First comes a philological discussion of the proposal to derive *algebra* from the name Geber, a discussion which is at the level of seventeenth-century standard philology at its best. Caramuel objects that Geber Hispanus (Ja bir Ibn Alfa) must have lived around the twelfth century, which is too late. But then Caramuel goes on, at first with a borrowing from Alsted's *Encyclopaedia* [43: III, 844a]:

*Algebra is an arabic word, which means the doctrine of the excellent man: AL, indeed, is the article: GEBER means Man: and it is often a title of honour, as with us Master, or Doctor. Today this book is much venerated among the erudite nations of the Orient, and by the Indians who are very fond of this art it is called Aliabra, or Alboret, since they do not know the proper name of its creator.*²⁵ Certainly rbg, GABAR, in Arabic is restored. And as the article is ל א, AL, prefixed, the restoration of arithmetic was א ל ג ב ר א.

²⁴ The other standard etymology derives the word from Portuguese *barroco*, an imperfect pearl. As far as metaphorical value is concerned, one explanation is as plausible as the other (which certainly would have pleased Caramuel if the word in its current meaning had existed in his times).

²⁵ Here the first borrowing from Alsted ends.

But why do we call the same science *coſſic*, and the ſpecial numbers which it makes uſe of, *coſſic numbers*? In Tome 2, book 14, chapter 4, § 1 in Alſted: *Moreover, Algebra was called the art of reſ, and cenſus by certain Latin writers; as with Regiomontanus; by the Italians (read, by the Spaniards)*²⁶ *Arte de la coſa, from which Coſſa. Chriſtoph Rudolph, excellent maſter of this art, conſiders that the rule is called Coſſic, as Art of things, becauſe it ſerves to ſolve queſtions about hidden things: after the manner in which arithmetic books uſually expreſs themſelves in all problems, We lay down a thing. Further, by certain Greeks Algebra was called Analytica. They alſo, etc.*²⁷ [...] And there are in Europe two current names, *Regula di tre* [the rule of three], and *Arte de la Coſa*, the former Italian, the latter Spaniſh, which clearly indicates how much theſe two nations have promoted, adorned and made illuſtrious arithmetic.

Further, if you do not want to favour the Spaniards, you ſhall ſay that the term *Coſſa* comes from the Hebrews or the Arabs to the Greeks and the Latins. Indeed קסר , *Caſar*, with the Saracens is to *Break* [*Frangere*], and therefore ſhould mean the ſcience which conſiders broken numbers [i.e., fractions]. Add to this that one may derive an etymology from the roots קצז *QAZA*, *Judged*, and קצר , *QAZAR*, *was Brief*: indeed, this ſcience is a kind of arithmetic which is fit for judging, and moſt ſure in matters concerned with numbers. An indication that it ſolves with utmoſt ſecurity and concision difficulties which ordinary arithmetic is hardly able to ſolve when moved in roundabout ways and labyrinths.

Johannes Geysius²⁸ explains the word differently. In *Book 1 on the Coß*, chapter 1, he ſays, *COSSA comes from קסר, CASA, that is, Weaved; it teaches indeed to find a number which has been hidden. Etc.* This indeed I do not underſtand, ſince “to weave” [*texere*] is not “to reveal” [*detexere*]. Say thus that this ability was named from weaving becauſe it diſentangles numbers which have been woven together and intertwined; ſo that the denomination refers not to the ſcience but to the object.

²⁶ This correction is inserted by Caramuel, who has not forgotten his Spanish origin even though he is a bishop in southern Italy. According to my work on the beginnings and background of Italian abbas algebra Caramuel may indeed be right in as far as the first algebraic use of the word is concerned.

²⁷ Alsted goes on “They also called normal arithmetic synthetic”, and explains that with reference to other works from the Ramist tradition.

²⁸ A parson [44: 220] and, as we see, amateur mathematician at the *Rechenmeister* level, who wrote 10 pages (vol. III, pp. 865–874) on algebra in Alsted’s encyclopedia. Alsted refers to him as *coſſiſta*.

In Greek it can also be called ΚΟΣΙΚΗ, since ΚΟΣΙΜΒΟΣ is a *Knot*.²⁹ And actually, all problems which are treated by this science are knots which you cannot solve if not by breaking (dividing unity). And also, if anybody is audacious, from *Cos*, a Latin word, *Cossica* is almost as saying *Cotica*. The mind actually needs a whetstone [*cos*] in order to be sharpened, and this science sharpens the mind, which is often dulled by badly digested methods. But even the small worms which bore through the hardest tablets are called *Cossi* by the writers on natural history. Also, if anybody is audacious, the name may be drawn from here. Indeed, if the multiplication table is easy and can be penetrated by any mind, others are hard, and cannot be penetrated if not by learning the *Cossic* art.

Further, it follows from Johannes Geysius's *Book 1 on the Coß*, chapter 4 No. 4 that *Coß* and *Algebra* are the same thing. There he says, *It is also called* ALMUCABALA, *that is*, Hidden tradition; *and also* ALGEBRA, *that is*, Magisterial Art. Etc. And Alsted, who in *Tome 2 book 14 § 1* says, *It is told that there was one remarkable Mathematician, who wrote down his art in Syriac language and sent it to Alexander the Great, and called it* ALMUCABALA, *that is*, *book on hidden things (this Art, indeed, teaches how to find a hidden number), the doctrine of which others preferred to call* ALGEBRA. None of them expresses the precise meaning of the word. Indeed, קבלה is *Tradition*, from the root קבל QABAL, *to transmit*. Since they would not divulge it, they did not transmit it in writing but orally to disciples. מקבלים MAQBALIM are *Cabalists*, and when the article is added it could be called AL-MUCABALA, not in Syriac but in Arabic.

ΕΝΑΡΙΘΜΟΣ is said about the one who is appreciated, a distinguished and extraordinary man: from which ΕΝΑΡΙΘΜΙΚΗ, some noble and distinguished kind of arithmetic, which is appreciated by learned men.

But one may also call this thing ΜΕΤΑΡΙΘΜΙΚΗ which has gone beyond the measure of common arithmetic and traverses the fields that lay beyond it.

It should be obvious that Caramuel does not believe that the etymologies from *Casar* onwards are historical truth. They are propounded for the case “you do not want to favour the Spaniards”; some are “audacious”, and repeatedly two alternative explanations are combined into one figure (as

²⁹ The spelling ought to be κοσύμβος, which actually is something made from knots (a hair-net etc.); but Caramuel's translation agrees with that of dictionaries from his century.

qaza and *qazar*). As the steganography and the logogriph, these etymologies are meant through poetical play to dig out – or rather display – aspects of the nature of algebra. That these aspects are indeed prior to the etymologies can be seen for instance from the example ΚΟΣΙΚΗ/κοσύμβος: only the one who already knows that he wants to get to broken numbers (that is, to transcend the Greek concept of number as a plurality of units) will find it in *knot*.

The Reception

As we see, Caramuel's *Mathesis biceps* is soaked with ambiguous and poetical Baroque subjectivity – so far removed from the Counter-reformation “constraint of consciences” that only familiarity with the mediating process allows us to discern the connection. Caramuel's Baroque is no external aspect, no mere decoration, as Grassi's poetical references in the treatise about the comets: it inspires the investigation of the “plurality of arithmetics” and allows the understanding of algebra as an abstract version of the false position. Even when writing about mathematics, Caramuel remains a Baroque mind.

Was he a mathematician all the same? The creators of the New Science appear to have nourished some doubts – as Vernet points out, they did not understand the new mathematical ideas contained in the *mathesis biceps* (Leibniz had to reinvent the place-value system), and the rest did not interest them. If we look for references to Caramuel in Oldenburg's correspondence³⁰ we do not find much. In 1668 John Collins (vol. V, p. 213) lists his *Solis et artis adulteria* as one of those books in a catalogue “which I do not much desire unless cheape”; in 1669 (vol. VI, p. 228) he asks Oldenburg “how he approves the treatises of John Caramuel Lobkowitz Intituled Ingeniorum crux et Mathesis audax”. Oldenburg (vol. VI p. 234) forwards the question to René-François de Sluse, who answers (vol. VI, p. 525) that “I saw the *Mathesis audax* and *Sublimium ingeniorum crux* very many years ago, but saw them only, nor does any memory of them remain”. In 1670 Sluse offers (vol. VII, p. 256) to get hold of the *Mathesis biceps*

³⁰ [45]. Where the letters are in Latin I quote from the stylistically faithful English translation of the editors.

when it becomes available. In the meantime, Oldenburg has received a letter from François Vernon (vol. VII, p. 273), which refers to

a great Vast Bulke of Caramuel, Able to fill a Library. His Mathesis biceps, speculative & Practicall [*sic*] 2 vol in Folio. His Calamus 2 volumes more [i.e., *Metametricala*] & whc is worse hee is [not] contented with the loade hee hath laid on the world already. but he promiseth to Plague it wth I doe no know how many volumes more.

In consequence, Oldenburg answers (vol. VII, p. 368) that

As for the two ample volumes of Caramuel Lobkowitz, we understand them to be damned with faint praise, which has cooled our desire to see them.

Sluse, on his part, concludes (vol. VII, p. 484) after getting hold of the volumes that

I have looked through Caramuel's farrago, and indeed, to speak kindly, its utility does not seem proportionate to its bulk.

This was all – neither much nor very positive.

Historical or historiographical problem?

An examination of Kircher's works and their reception would lead to similar results. Most of his works about nature deal with issues and objects for which it was less easy to judge the validity of new results and proposals than in the case of mathematics – magnetism, the subterranean world, applied acoustics – so the rejection is less absolute. Yet the difference is not significant – when Kircher approached nature as a *Gesamtkunstwerk* or *theatrum* it was difficult to find a perspective which was theoretically fruitful or seen as such by the representatives of the New Science.

In so far we may say that the absence of a Baroque impact on the New Science is a fact of history, no historiographical blind spot. Works which were too close to the Baroque current with its emphasis on ambiguity and poetico-connotative understanding were too far removed from the sensibility of the New Science to gain much influence. When they offered new answer, these were to questions which seemed outdated or irrelevant, or

they concerned matters that were too complex to allow the answers to be convincing.

However, once work with the Baroque prototypes (not “ideal types”, since Caramuel and Kircher were quite real!) has opened our eyes to characteristic Baroque features, we may find such features elsewhere though as a rule not together. I shall not go into details but just suggest three sketchy examples.

First we may think of Scott Mandelbrote’s distinction between two kinds of natural theology in seventeenth-century England [46]: on one hand the “Wilkins-Boyle” type which

stressed the importance of the providential ordering of nature and the consequent lawful operation of the universe as a proof of divine superintendence and of the power of the divine will

on the other that of the Cambridge Platonists, which based its argument on

appeal to the wondrous activity found in nature, of which regularity was only ever a part, and which required the constant, creative involvement of a hierarchy of spiritual agents

and which

was ultimately weakened by its association with credulity and with discredited attempts to prove that spiritual agents could be observed at work in the world.

The spiritual agreement of the latter group with the Kircher we know for instance from the *Musurgia universalis* is not perfect, nor is it however totally absent. The reasons for rejection are also fairly alike.

Next, we may turn our attention to the title pages and frontispieces of scientific printed works of the epoch. The point is not that these look very much like other visual art from the epoch, and thus as “Baroque”; this could hardly be otherwise.³¹ Significant is that they served to carry a message by indirect, metaphorical means about the trustworthiness and legitimacy of the book under the frontispiece. As stressed by Volker Remmert [47], however, the message of the frontispiece was not only distinct from the

³¹ Similarly, Eriksson’s observation that “we must admit [the] striking baroque character of Newton’s monument in the Westminster Abbey” [2: 164] is irrelevant as an argument for declaring Newton a Baroque scientist.

technical argument of the book, which it would indeed be hard to translate into emblematic pictures; it was also largely directed at a different audience, an audience that was hardly able to follow the technical discourse. The text of books was thus directed at the argument-based public sphere of what was soon to be called the “republic of letters”, whereas the frontispieces – which were indeed so detached from the argument of the book for which they were produced that they might be transferred to quite different books – were directed at a distinct, representative public sphere.

We may finally ask whether the tenacious dedication of certain late-seventeenth and early-eighteenth-century *virtuosi* to the study of insects, worms and microscopic animals irrespective of the scandalized antagonism of galant society and writers like La Bruyère and Addison [48: 29f and *passim*] can not be seen as a symptom of Baroque obsession with everything proteic.

If such suggestions of Baroque presence are taken into account, we may conclude that the total absence of the Baroque from the historiography of seventeenth-century science is also to some extent a historiographical artefact. But this is a different story which I shall not pursue.

A third story – no less important, perhaps, but which I shall not take up even sketchily – is the *modernity* of the Baroque. Not, of course, in relation to modern *science*, but as the starting point for an understanding of the nature and tasks of poetry that was to unfold in the aesthetic theory of the twentieth century (see [49] and [50]) – and (less flattering perhaps for the seventeenth century but quite to the point if we think of the initial intertwinement of the Baroque with Counter-reformation propaganda) in relation to the contemporary calculated use of emotion, ambiguity and indirect messages in the advertisement industry.

References

- [1] Rudbeck, Olaus, *Atland Eller Manheim. Dedan Japhets afkomne, de förnemste Keyserlige och Kongelige Slechter ut til hela werlden, henne at styra, utgångne äro, så och dess efterföljande Folk utogade, nemligen Skyttar, Borbarn, Asar, Jettar, Giotar, Phryger, Trojaner, Amaizor, Traser, Lyber, Maurer, Tussar, Kaller, Kiempar, Kimrar, Saxer, Germen, Swear, Longobarder, Wandaler, Herular, Gepar, Tydskar, Anglar, Paitar, Danar, Sidkampar, och de som i werket wisas skola. Atlantica Sive Manheim. Vera Japheti posterorum sedes ac patria, ex qua non tantum*

- Monarchae et Reges ad totum fere orbem reliquum regendum ac domandum, Stirpesque suas in eo condendas, sed etiam Scythae, Barbari, Asae, Gigantes, Gothi, Phryges, Trojani, Amazones, Thraces, Libyes, Mauri, Tusci, Galli, Cimbri, Cimmerii, Saxones, Germani, Svevi, Longobardi, Vandali, Heruli, Gepidae, Teutones, Angli, Pictones, Dani, Sicambri, aliique virtute clari et celebres populi olim exierunt.* Uppsala: Henricus Curio S.R.M. & Academiae Upsal. Bibliopola, [1679].
- [2] Eriksson, Gunnar, *The Atlantic Vision: Olaus Rudbeck and Baroque Science*. (Uppsala Studies in History of Science, 19). Canton, Mass.: Science History Publications, 1994.
- [3] Høyrup, Jens, “Barocco e scienza secentesca: un legame inesistente?” *Analecta Romana Instituti Danici* 25 (1997), 141-172.
- [4] Høyrup, Jens, “Reflections on the Baroque in the History of Science”. Essay Review of: Gunnar Eriksson, *The Atlantic Vision: Olaus Rudbeck and Baroque Science*. *Physis* 24 (1997), 675-694.
- [5] Hooykaas, R., *Humanisme, science et réforme: Pierre de la Ramée (1515-1572)*. Leiden: Brill, 1958.
- [6] Hofmann, Joseph Ehrenfried, *Geschichte der Mathematik*. 3 Bände. (Sammlung Göschen 226, 875, 882). Berlin: Walter de Gruyter, 1953, 1957, 1957.
- [7] Wellek, René, “Baroque in Literature”, pp. 188-195 in *Dictionary of the History of Ideas*, vol. I. New York: Scribner, 1973.
- [8] *Grande dizionario Garzanti della lingua italiana*. Milano: Garzanti, 1987.
- [9] Hauser, Arnold, *Il Manierismo. La crisi del Rinascimento e l’origine dell’arte moderna*. (Biblioteca di storia dell’arte, 4). Torino: Einaudi, 1965.
- [10] Wittkower, Rudolf, *Arte e architettura in Italia: 1600-1750*. (Biblioteca di storia dell’arte, 14). Torino: Einaudi, 1972.
- [11] Waterworth, J. (ed., trans.), *The Canons and Decrees of the Sacred and Oecumenical Council of Trent*. London: Dolman, 1848. Pp. 232-289, “Twenty-fifth Session” on <http://history.hanover.edu/texts/trent/ct25.html>.
- [12] Ginzburg, Carlo, *Il formaggio e i vermi: Il cosmo di un mugnaio del ‘500*. Torino: Einaudi, 1976.
- [13] Mullan, Elder (ed., trans.), *The Spiritual Exercises of St. Ignatius of Loyola*, translated from the autograph. New York: P. J. Kennedy & Sons, 1914. <http://www.ccel.ignatius/exercises/formats/exercises1.0.pdf>.
- [14] de Loyola, Ignacio, *Ejercicios espirituales*. Barcelona: Linkgua, 2007.
- [15] Barocchi, Paola (ed.), *Scritti d’arte del Cinquecento*. 9 vols. Torino: Einaudi, 1978.
- [16] John Donne, *Selected Poetry and Prose*, ed. T. W. Craik & R. J. Craik. London & New York: Methuen, 1986.
- [17] Drake, Stillman, & C. D. O’Malley (eds, trans.), *The Controversy of the Comets of 1618. Galileo Galilei, Horatio Grassi, Mario Guiducci, Johann Kepler*. Philadelphia: University of Pennsylvania Press, 1960.
- [18] Farrington, Benjamin, “Prometheus Bound: Government and Science in Classical Antiquity”. *Science and Society* 2 (1937-38), 435-447.
- [19] Hacking, Ian, *The Emergence of Probability*. London: Cambridge University Press, 1975.

- [20] Caramuel, Juan, *Apologema pro antiquissima et universalissima doctrina, de probabilitate. Contra novam, singularem, improbabilemque D. Prosperi Fagnani opinionationem*. Lyon: Sumptibus Laurentii Anisson, 1663.
- [21] Pascal, *Oeuvres complètes*, ed. Jacques Chevalier. (Bibliothèque de la Pléiade, vol. 34). Paris: Gallimard, 1954.
- [22] Eamon, William, "Court, Academy and Printing House: Patronage and Scientific Careers in Late Renaissance Italy", pp. 25-50 in Bruce T. Moran (ed.), *Patronage and Institutions. Science, Technology and Medicine at the European Court, 1500-1750*. Rochester, New York: Boydell & Brewer, 1991.
- [23] Josten, C. H., "A Translation of John Dee's 'Monas hieroglyphica' (Antwerp, 1564), with an Introduction and Annotations [and a facsimile of the Latin text]". *Ambix* 12 (1964), 84-221.
- [24] della Porta, Giovanni Battista, *Magiae naturalis libri viginti*. Frankfurt, Wechel, 1591.
- [25] Høyrup, Jens, "From Hesiod to Saussure, from Hippocrates to Jevons. An Introduction to the History of Scientific Thought". Eighth, still preliminary version. *Lecture notes*, Roskilde Universitetscenter, Faggruppen for Filosofi og Videnskabsteori, 2004.
- [26] Long, Pamela, "The Openness of Knowledge: An Ideal and Its Context in 16th-Century Writings on Mining and Metallurgy". *Technology and Culture* 32 (1991), 318-355.
- [27] Høyrup, Jens, "Erkendelsesteoretiske, historiske og andre bemærkninger til offentlighedsbegrebet". *Filosofi og Videnskabsteori på Roskilde Universitetscenter* 4 (1984), 136-168.
- [28] Foley Ames, M. G. (ed., trans.), Otto von Guericke, *The New (so-called Magdeburg) Experiments*. [Experimenta nova, Amsterdam 1672]. (Archives Internationales d'Histoire des Idées, 137). Dordrecht etc.: Kluwer, 1994.
- [29] Krafft, Fritz, "Guericke, Otto von", pp. 574-576 in *Dictionary of Scientific Biography*, vol. V. New York: Scribner, 1972.
- [30] Middleton, W. E. Knowles, *The Experimenters: A Study of the Accademia del cimento*. Baltimore: Johns Hopkins Press, 1971.
- [31] Caramuel, Juan, *Steganographiae, nec non claviculae Salominis Germani, Ioannis Trithemii, genuina, facilis dilucidaque declaratio*. Köln: Typis Egmondanis, 1635.
- [32] Brann, Noel L., *Trithemius and Magical Theology: A Chapter in the Controversy over Occult Studies in Early Modern Europe*. Albany, NY: SUNY Press, 1999.
- [33] Coulianu, Ioan P., *Eros and Magic in the Renaissance*. Chicago: Chicago University Press, 1987.
- [34] Caramuel, Juan, *Mathesis biceps. Vetus, et nova*. 2 vols. Campania: In Officina Episcopali, 1670.
- [35] Caramuel, Juan, *Primus Calamus ob oculos ponens Metametricam*. Romae: Fabius Falconius, 1663.
- [36] Lüthy, Christoph, "Where Logical Necessity Becomes Visual Persuasion: Descartes's Clear and Distinct Illustrations", pp. 97-133 in Sachiko Kusukawa & Ian

- Maclean (eds), *Transmitting Knowledge: Words, Images and Instruments in Early Modern Europe*. Oxford: Oxford University Press, 2006.
- [37] Gavilán, María Dolores Martínez, “La *Grammatica audax* de Juan Caramuel y las corrientes lingüísticas del siglo XVII”, pp. 107-133 in E. F. Koerner & Hans-Josef Niederehe (eds), *The History of Linguistics in Spain II*. Amsterdam: John Benjamins, 2001.
- [38] Pérez de Laborda, Alfonso, *Estudios filosóficos de historia de la ciencia*. Madrid: Encuentro, 2005.
- [39] Vernet, Juan, “Caramuel y Lobkowitz, Juan”, p. 61 in *Dictionary of Scientific Biography*, vol. III. New York: Scribner, 1971.
- [40] Newton, Isaac, 1728. *La Chronologie des anciens royaumes corrigée, à laquelle on a joint une chronique abrégée, qui contient ce qui c’est passé anciennement en Europe, jusqu’à la conquête de la Perse par Alexandre le Grand*. Paris: Gabriel Martin, Jean-Baptiste Coignard, Hippolite Louis Guerin & François Montalant, 1728.
- [41] Rodet, Léon, “Les prétendus problèmes d’algèbre du manuel du calculateur égyptien (Papyrus Rhind)”. *Journal asiatique*, septième série 18 (1881), 184-232, 390-559.
- [42] Ineichen, Robert, “Leibniz, Caramuel, Harriot und das Dualsystem”. *Mitteilungen der Deutschen Mathematiker-Vereinigung* 16:1 (2008), 12-15.
- [43] Alsted, Johann Heinrich, *Encyclopaedia. 7 tomis distinctis*. Herbornae Nassoviorum, 1630.
- [44] Hotson, Howard, *Commonplace Learning: Ramism and its German Ramifications, 1543-1630*. Oxford: Oxford University Press, 2007.
- [45] Hall, A. Rupert, & Marie Boas Hall (eds, trans.), *The Correspondence of Henry Oldenburg*. 13 vols. Madison, Wisconsin: University of Wisconsin Press (I-IX) / London: Mansell (X-XI) / London & Philadelphia: Taylor & Francis (XII-XIII), 1965-1986.
- [46] Mandelbrote, Scott, “The Uses of Natural Theology in Seventeenth-Century England”. *Science in Context* 20 (2007), 451-480.
- [47] Remmert, Volker R., “‘Docet parva pictura, quod multae scripturae non dicunt.’ Frontispieces, Their Functions, and Their Audiences in Seventeenth-Century Mathematical Sciences”, pp. 239-270 in Sachiko Kusukawa & Ian Maclean (eds), *Transmitting Knowledge: Words, Images and Instruments in Early Modern Europe*. Oxford: Oxford University Press, 2006.
- [48] Daston, Lorraine, *Eine kurze Geschichte der wissenschaftlichen Aufmerksamkeit*. (Themen, 71). München: Carl Friedrich von Siemens Stiftung, 2002.
- [49] Koch, Ludovica, “Rime, arditezze e ragioni”, pp. 169-194 in *Etimologia: Pratiche e invenzioni* (Fabrica 1. Quaderni di retorica e di euristica letteraria). Napoli: Istituto Universitario Orientale, 1983.
- [50] Koch, Ludovica, “Écho, sa raison et ses rimes”, pp. 89-96 in Inge Degn, Jens Høyrup & Jan Scheel (eds), *Michelanea. Humanisme, litteratur og kommunikation*. Festskrift til Michel Olsen i anledning af hans 60-årsdag den 23. april 1994. (Sprog og kultur-møde, 7). Aalborg: Center for Sprog og Interkulturelle Studier, Aalborg Universitetscenter, 1994.

Laudatio Pia Letto-Vanamo

M. Maresceau

Prof. Letto-Vanamo was born in Rovaniemi in the North of Finland. She studied law at the University of Helsinki. After her graduation she became a research associate at the Finnish Academy and university assistant. She prepared a PhD research on “The Beginning and Early History of the Finnish Legal Profession” and obtained her doctorate in 1989. Afterwards she became assistant professor in History of Law at the University of Helsinki and guest researcher at the Max-Planck-Institut für Europäische Rechtsgeschichte in Frankfurt am Main. In 1991 she was appointed professor in Roman Law and History of Law at the University of Helsinki.

In 1997, while continuing various teaching commitments in History of Law, she was also attached to the Institute of International Economic Law of the University of Helsinki. In 1999 she received the Jean Monnet Chair at the same university, which implied a strong orientation of her academic activities towards EU affairs, in particular EU law. In 2001 she became Director of the Institute of International Economic Law. Recently, she was also appointed Director of the University of Helsinki Graduate School “Foundations of European Law” and became Co-Director of the international research team “Europe as a Market” in the Centre of Excellence for Foundations of European Law and Polity Research. In addition, from 1997 to 2003 prof. Letto-Vanamo was President of the Finnish European Studies Association and in that capacity she was and is a prominent and very active member of ECSA (European Communities Study Association) World.

Prof. Letto-Vanamo was regularly *extra muros* member for doctoral dissertations in Finland and abroad and taught as a visiting professor at various foreign universities.

The fields of research of prof. Letto-Vanamo are: history of law and in particular European legal history, the history of the legal profession, the Nordic legal tradition with, of course, a strong emphasis on the specific position of Finland. Within this topic, “access to justice” occupies a prominent place. But, – and this may appear rather astonishing – prof. Letto-Vanamo has been able to combine these initial research fields with a strong orientation of her academic and scientific activities towards European Union law, one of the new branches in the field of law.

Within the area of European Union law, the focus is on the “Third Pillar”, that is the law related to Justice and Home Affairs. The “rule of law” and its role in the broad European legal tradition as a fundamental principle of the European Union receive particular attention and one of her important publications has as a title: “Rechtsstaat als Kriterium für Europa”. It is well-known that respect of the “rule of law” in the political and legal conditions for membership of the European Union, as launched by the 1993 European Council of Copenhagen, is one of the most important considerations in the assessment of a Candidate State’s ability to become EU member.

It is totally impossible in this *laudatio* to provide an exhaustive list of prof. Letto-Vanamo’s publications. Only a few ones can be mentioned here: *History of Assistance in Conflict Resolution in Finland*, Helsinki, 1994; *Beginning and Early History of Finnish Legal Profession*, 1989; *Europe in Law. Lectures in Legal History*, Helsinki, 1995; *The Law of the Ting Community. The Jurisdiction in Sweden-Finland Before the Stabilisation of the Conflict Resolution of the State*, 1995; *Europe as a Legal Community and Possibilities for Co-operation*, Helsinki, 1998; *Access to Justice: A Conceptual and Practical Analysis with Implications for Justice Reforms*, 2005; *Moments of Finnish Justice in the 1970’s*, 2005.

The proposal to award the Sarton Medal to prof. Letto-Vanamo received an enthusiastic and unanimous response from the Law Faculty of Ghent University and the Sarton Committee. The unexpected combination of history of law on the one hand with the process of European integration and cooperation on the other hand makes of prof. Letto-Vanamo a very special, yes indeed unique, laureate. She is one of the very rare law professors who has successfully been able to combine these two at first sight totally different worlds. The most appropriate manner for the Law Faculty to pay

tribute to our colleague prof. Letto-Vanamo for such a “tour de force” was – how could it be else? – the Sarton Medal Award. We are delighted and honoured that she has accepted the Award and that she is today among us to give a lecture on “Law, History and European Integration”.

Law, History, and European Integration

Pia Letto-Vanamo

University of Helsinki

1. Introduction: The title of my paper is “Law, History, and European Integration”. The subtitle, however, could be “Some Ideas for Rethinking European Law”. Actually, it is quite popular to “rethink” – at least among my colleagues in the Nordic Countries. Indeed, some weeks ago I gave a speech at the University of Copenhagen at a conference arranged by my Danish colleagues in legal history, legal theory, and legal sociology. The topic of the conference was “Rethinking European Legal Culture”. Then, too, my faculty at Helsinki has a Centre of Excellence for Foundations of European Law and Policy Research (see: <http://www.helsinki.fi/katti/foundations/>), where the main goal is to rethink European law, especially as far as concerns the current doctrine of legal sources and legal reasoning.

Evidently, my Nordic colleagues are right in their rethinking approach. Generally speaking, we – working and studying at universities – should always be capable of and ready for rethinking, for seeking new perspectives, for questioning old truths. More specifically, European integration is challenging us to new narratives of the history of European Law, and to new ideas about its future, particularly with the enlarged European Union.

I have three main points in my paper: First, I will deal with European legal history, about a definition of a *Europe of Law* that can be found in the writing and teaching of legal historians in most European countries. After that I will discuss the *law of Europe* by presenting some trends in current development of European Law, and claiming that:

- a) many European laws exist – or at least many different approaches to legal harmonization, which is true even within the European Union, and

- b) a trend is under way from substantive law to procedural law that can be seen in European regulation, both within the European Union and at national level, too.

Finally, I will comment on European justice (*Gerechtigkeit*), which is – or should be – something more than purely and simply European legislation.

2. What is Europe?: When we try to define Europe by reading books and articles written by historians, philosophers, or even political scientists we easily recognize how they all agree that Europe is not only a geographic unity, but it is also something ideal, something cultural.

At least three key elements defining European identity are mentioned. These are Christianity, Greek philosophy, and Roman law. And while studying texts written by legal historians, the most important foundation of Europe seems to be Roman law.

Thus, we are telling our students the story (hi-story) of European legal thinking by claiming that European legal systems have similarities – even a common core – based on the influence of Ancient Roman Law.

This story has been, and could be criticized; not only because of its euro-centrism, but also because it is told mainly by German legal historians, neglecting legal historical developments in the European “peripheries” such as those in the Nordic countries. However, it is quite a good story, a great narrative of the importance of law in Europe. The most crucial point in the heritage of Ancient Roman Law is the idea of an autonomous normative (consequently legal) order regulating relations between human beings.

That is something European, which becomes clear when comparing European legal tradition(s) with other legal traditions of the world. Of course, even in Europe legal norms do not emerge or function in a vacuum; and it would be impossible to think that a national or supranational legal order (especially with criminal law norms) could be efficient without reflecting the basic ethical and moral values of the society concerned.

It is not only the idea of law we have acquired from Ancient Rome. The most important institutions and concepts of modern European (private) law can be found in ancient literature: in the *Institutions* of Gaius and in the *Digest*, the second part of the Justinian *Corpus iuris civilis* from the 530s AD.

It also appears that European integration – the founding of the European Community in the 1950s – would not have been possible without countries with similar legal orders: sharing the same basic ideas concerning, for example, contract law and issues of liability.

Today, we see that the European Union is not only furthering economic integration. It is furthering legal integration, as well – by using legal instruments for the purposes of economic integration. And the law is also present as a criterion for membership of the Union. According to the so-called Copenhagen criteria, only states respecting the principle of the rule of law (*Rechtsstaat*) can become members of the EU. Thus, the law is also important for economic relations, for a well-functioning market economy, and for co-operation between state authorities.

You may remember how Max Weber, one of the big names in European legal and political thinking, wrote about “the European way” by maintaining that the big cities with their economically active bourgeoisie were crucial for the modernization of law in Europe. Predictability was and is of importance in economic relations; and this can be guaranteed through legal norms and their application by independent courts.

But where European integration is concerned, it is not the idea of law – or law as an instrument – that is important. Additionally, the so-called second life of Roman law used to be mentioned, at least for educational reasons. Then the focus was on the history of European universities and the reception of Roman law. We learned that many still-functioning European universities, such as the Universities of Bologna, Paris, Montpellier, Cologne, and Prague, were founded in the Middle Ages. We also know that in all of them it was usual to study law – both Roman law and Canon law.

Researchers of university history have told us that the medieval universities, their teachers and students, formed an early European network of law – that of trained lawyers. They read the same books, compiling and commenting on Ancient Roman law texts. The same teaching method, the scholastic method, was used, the Latin language was the *lingua franca* of university education, and very often students and professors were travelling around Europe, moving from one university to another. Researchers interested in the history of the legal profession have found that those universities trained young men as judges, secretaries (often with the title of *syndicus*) or advocates mentioned in the court records of the big cities or in

the early high courts. They were representatives of the European *ius commune*, the Roman-Canon common law.

However, this narrative can also be criticized. At least, it should be mentioned that many variations existed of the European Roman-Canon *ius commune*, like today with European Community/Union Law. Additionally, it can be claimed that legal scholars always have double citizenship. We learn – and are inspired by – foreign theories and ideas, but we are also practitioners: Legal ideas will be tested through legal practice, and international ideas such as new European legal principles or concepts have to be transposed into national environments in light of relevant societal and economic conditions.

3. (a) Nevertheless, that (hi)story contains something very interesting. In the Middle Ages, Ancient Roman law was not only taught and learned – it was also reformed and systematized. Canon law became systematized, as well. Since then, we have had many common classifications, categories, and concepts in European legal science(s). Roman law has been important for development of private law doctrine. Ideas and concepts from Canon law cannot be denied where the history of public or criminal law is concerned. For instance, the principle of subsidiarity – crucial for today’s EU Law – was developed by canonists.

And it is this period of European legal history that has mostly inspired scholars of today – at least those interested in harmonization of current European law on the basis of common European principles, common concepts, and of common European legal education. This can be called a model of bottom-up-harmonization. This model has inspired most academic working groups for European legal harmonization, such as the Lando Commission drafting Principles of European Contract Law (PECL), or the Acquis Group (European Research Group on Existing EC Private Law), or the group of professors that recently drafted and published (in cooperation with the European Commission) a Draft Common Frame of Reference (DCFR; Principles, Definitions and Model Rules of European Private Law).

These academic groups have so to say an opposite agenda to that of the EU legislator with “sending” often quite fragmented competition, consumer, and other norms (regulations and directives) to Member States, where

national state authors with the help of legal professionals try to place them into the national legal order and implant them into the national legal doctrinal system. This can be called a top-down-approach to European harmonization.

But still other approaches exist to European legal co-operation, even within the European Union. We all know something about international private law, about its system based on complicated choice of law rules and the principle of *ordre public* protecting basic values of the national legal order/society concerned.

You might also know of quite a new EU Regulation called the Rome I Regulation (EC 593/2008) on the law applicable to contractual obligations (based on the Rome Convention, 1980). The regulation includes, for example, rules on freedom of choice and on the applicable law in the absence of choice. Astonishingly, this contains no references to the Principles of European Contract Law (PECL) or to the UNIDROIT Principles of International Commercial Contracts (2004). However, in a workshop in Helsinki two weeks ago (December 2008) one of the drafters of the Regulation stated that it was the will of the EU Member States not to open up the use of bottom-up-drafted principles. These are made by law professors – not through the democratic legislative procedure of the European Union.

Thus, competing approaches exist to harmonization of European law. Apart from law professors, national states, the European Parliament, and the European Commission, at least one other actor interested in development of European (Union) law has to be mentioned. This is the EU judiciary. Today, the European Court of Justice is – perhaps not “running wild”, but playing a crucial role by widening the scope of European Union Law. This can especially be seen when human rights and other basic rights are concerned.

At least one ECJ case ought to be mentioned. This is the so called *Kadi* case (*Yassin Abdulla Kadi and Al Barakaat International Foundation against the Council and Commission; Joined Cases C-402/05 P and C-415/05 P*). Through this case, the European Court of Justice is re-defining the relationship between international law and EU law – by annulling a Council Regulation based on a Resolution of the Security Council of the United Nations, because it infringes Kadi’s and Al Barakaat’s fundamental rights under European Community Law.

3. (b) It is not substantive law that seems to be important for the Europeanization of law. And it is not the European Union that has been the agent of legal harmonization in Europe. The Council of Europe, the European Convention on Human Rights (1950) and the European Court of Human Rights ought to be mentioned here, as well.

In my country, entry to the European Union (in 1995) was no legal revolution, but ratification of the European Convention on Human Rights (1990) was – at least a small one. Article 6 of the Convention on the right to a fair trial was the main reason for a deep-going reform of the Finnish court system and legal procedure in the 1990s. Indeed, several cases against Finland in the Strasbourg Court have dealt with the requirement of Article 6 §1 that a decision must be made within a reasonable time.

Further, many other EU countries – not only new Member States – have been on the receiving end of judgments from the Court of Human Rights based on Article 6 concerning, for example, access to justice, independence of the judiciary, and parties' right to be heard.

At the same time, it is interesting to look at current documents of European Union institutions. There, terms such as good governance, better regulation, co-regulation, or alternative dispute resolution, European ombudsman, and so on, are commonplace. Often, they refer to the fact that decision-making procedures are also important, or at least that a need exists for new models of regulation or decision-making.

In my understanding, this can be seen as a sign that justice is also emerging through certain procedures, by applying certain formalities. In every case, an interesting idea lies behind the trend: the experience or the hope that citizens (parties to a case) may accept negative decisions if they have had a real opportunity to participate in the decision-making (or court) procedure, i.e. they have been properly heard, and fairly treated.

From the perspective of legal history, however, this is nothing new. It is well known that during pre-modern times people gathered together in early court sessions, at the so-called *thing*, to talk of common matters and to resolve conflicts. And although no adjudicating third party, no authoritative sovereign, stood above the parties, nevertheless decisions made by the *thing* assembly acquired acceptance or legitimacy. This happened through participation – and through use of certain formalities (rituals), as well.

4. However, justice has never been, and cannot be only something procedural. This is true especially when justice in the meaning of *gerechtigheid* is concerned. Then, one can ask whether a place exists for justice in European Union Law – or even more widely, in current European legal thinking.

To answer this question I would like to refer to an interesting debate, to that between *Paolo Prodi* and *Jan Schröder* on the relationship between law and justice. In his great book “Una Storia della Giustizia” (2000, translated into German 2003) Italian historian Paulo Prodi claims that until early modern times several fora, and a pluralism of legal orders, existed, where (divine-) natural, secular, and ecclesiastical norms lived side by side. After the Reformation and the fall of Natural Law, pluralism changed to a monism of positive norms. Today, we stand solely in one forum, that of positive written norms.

At the same time, justice (*giustizia*) has retired into the individual conscience. Instead of a pluralism of legal orders, we are facing the dualism of positive law and conscience. According to Prodi, we are facing development towards a one-dimensional legal norm(ativity) without any meeting with justice. Today, no binding legal ethics exist that could help us to deal with the problems of our time. Thus, one can recognize the incompetence of the one-dimensional norm in handling justice, especially when questions about abortion, euthanasia, or protection of the environment are concerned.

In the article “Verzichtet unser Rechtssystem auf Gerechtigkeit” (Akademie der Wissenschaften und der Literatur 2/2005) German legal historian Jan Schröder criticizes Prodi’s pessimism with examples taken mostly from German legal history but also from current European debates, those on so-called general legal principles and fundamental rights.

It is true that, during the era of the (pluralistic or) dualistic legal system, injustice in positive law could be redressed by norms of Natural Law, or by *equitas* as one form of justice. In our time this is not possible, but correcting means are still available for a judge who regards positive law as unjust. Since the 18th century a model of unwritten legal principles has existed, the idea that positive law as such includes unwritten basics, so-called legal principles. According to modern theory (since the 20th century) legal principles surround positive law but with less binding force than that of ordinary legal norms. Today, we also know the model of legalistic justice, which covers modern fundamental rights and so-called general clauses of

individual laws. Moreover, judicial technique has changed over time. No longer are references made to justice as such, no use is made of “scientific legal sentences” as in the 19th century, but application of legal principles occurs – as “guidelines” from individual legal culture curing unjust positive law.

Thus, our time has not forgotten justice, but different techniques have been developed for bringing it within the modern legal system. These techniques are historically determined, and local variations in their use exist.

And still today, also according to Schröder, common or shared ideas of justice exist for measuring positive law. For instance, no concept of customary law could exist without collective ideas of justice. A custom can become legal only if it is derived from a certain understanding of law. Otherwise criminal customs could also become part of law. But often, in current complex European societies dominated by the law, only members of the legal profession have that understanding. Or at least they seem to have it: otherwise such institutions would not exist beside or against traditional ones such as national and international soft law – with e.g. the new *lex mercatoria* – based merely on ideas and acts of their own agents.

On the basis of historical analysis we can, like Paolo Prodi, point to the dominance of pure law and individualization of the idea of justice, but we can claim, like Jan Schröder, that the modern legal order also includes ideas of (objective) justice. In my understanding, it is possible to assert that collective ideas of justice are transported into European and national legal reasoning and decision-making through fundamental rights. Individualization is characteristic of modern ethics, but more consensus exists than before on fundamental moral norms, at least within European institutions. This can be seen in human and fundamental rights, where moral norms have been translated into legal language.

Thus, the law is needed if different values cause conflicts between individuals and groups. Then, legal principles, linked with fundamental and human rights, do not define values of individuals and groups but guide resolution of conflict between them. This can be seen, for instance, concerning freedom of speech or freedom of religion. Thus, human rights are guarantees for individual choices. And freedom of choice is one of the foundations of modern law.

Laudatio Paul Eling

Robert J. Hartsuiker

It is a great pleasure to introduce Paul Eling. The last time I saw Paul was about ten years ago, when he was an examiner of my doctoral thesis. I am glad to welcome him today under (at least for me) rather less stressful circumstances. Paul obtained his PhD in 1983 at what was then called the KU Nijmegen on a dissertation about laterality, a topic he was already interested in as a student at the same university. He was then appointed for two years as a researcher at the Max Planck Institute for Psycholinguistics on a project about aphasia. Since 1985 he is appointed as professor in neuropsychology at the Radboud University Nijmegen, and conducts research in a domain that has received a great deal of attention in recent years, namely the relation between brain and behavior. More specifically, his research focuses on the biological basis of attention and learning. He has published dozens of papers on this topic in scientific journals and he has supervised numerous PhD students.

But a second strand of Paul's research, and the reason why he is awarded the Sarton medal today, is his contribution to the documentation and analysis of the history of neuroscience, a topic on which he has also published dozens of papers. There are two major themes in this work. The first theme is the history of neuroscience in The Netherlands and the contributions of several key figures, such as Jacobus Schroeder van der Kolk, a contemporary of F. C. Donders. The second theme is the history of aphasiology; here Paul asks for example what Paul Broca and Carl Wernicke *really* said, and how their views fit in their historical context.

What is so interesting about this work? I will mention two aspects. First, as I said, the last two decades have shown an enormous increase in interest in

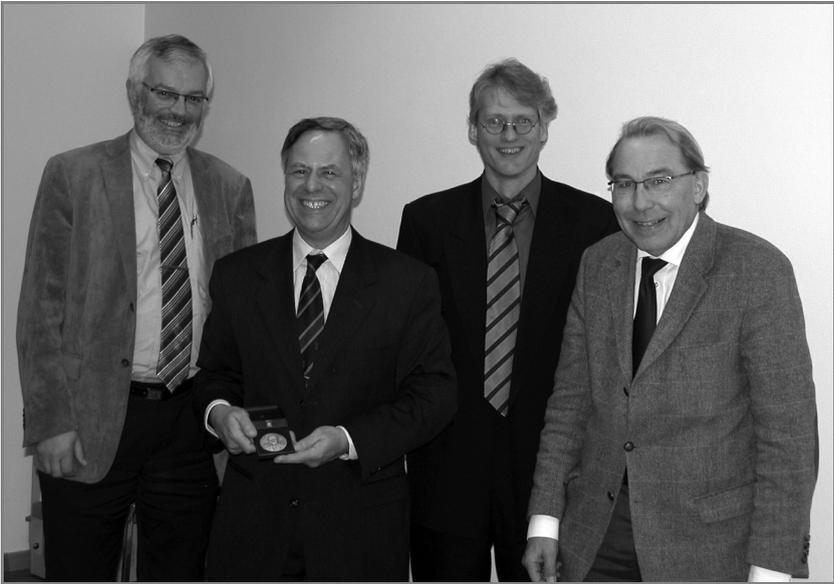
studies on the relation between brain and behavior. This is true for Academia, where the cognitive neurosciences have grown explosively, but also for the outside world. Indeed, it is difficult nowadays to open the science section of a quality newspaper, without being confronted with (sometimes nicely colored) pictures that show brain activity while a person is engaging in a certain behavior. To illustrate this, I conducted a search of the digital archive of *NRC Handelsblad* with keywords like “brain activity”, “brain scan”, and “fMRI”. This yielded dozens of hits, such as “male brain responds strongly to contempt”, “brain punishes abnormal judgment”, and “Chinaman calculates with different part of brain than Westerner”. It is perhaps not surprising that such strong statements evoke a response. The American philosopher Jerry Fodor sighs in the *London Review of Books* “*why, why does everyone go on so about the brain?*” Others speak unkindly about “chromophrenology”.

Although such comments often miss the point, they do illustrate the need for critical reflection. In Paul’s words “Because of the enormous amount of research that is conducted nowadays and the large pressure to publish more and more, there seems to be little time and little desire for reflection. Where are we now, what do all these findings tell us, which angles receive too little attention?” If one then considers the way the history of the field is typically portrayed, there seems to be a clear tendency to emphasize progress. Scholars describe how limited, or wrong, research in the past was, and in contrast how much we now know and how much we can now do. But if one *really* delves into the history of the field, it turns out that this progress idea is actually a misrepresentation. It is better to talk about a continuous alternation of viewpoints. An alternation, for example, between a period in which mind and body are considered as integrated, with a period of Cartesian dualism (according to some a false trail from which the field has only recently returned). And an alternation between a period in which the dominant view is that each part of the brain can do everything, with a period in which the dominant view is rather that specific mental functions can be localized in specific regions of the brain.

A second reason why Eling’s approach is interesting, is that one can obtain a much better understanding of certain positions from the past if one goes back to the original sources. Many scientists cite these sources, but without actually reading them. Eling’s investigations of the history of aphasiology

show that this practice can lead to serious misconceptions. A good example is one of Paul's first articles, in which he reveals '*What Broca actually said*'. This shows that for more than a century, claims have been attributed to Broca about the lateralization of speech and motor control in the brain which he in fact never made. Another example is a series of papers in which Paul addresses the origins of the famous model of Carl Wernicke. These papers read like a detective story. The trailer is this. Carl Wernicke, a young medical doctor, came to Vienna in the late nineteenth century to pursue a PhD with Theodor Meynert, who was famous for his work on neuro-anatomy. It was Wernicke's first introduction to aphasia. Half a year later, at the age of only 26, Wernicke published his world famous dissertation. This story raised several questions to Paul Eling. '*Isn't it odd that a young man, with no experience in aphasiology to speak of, publishes such an influential work in such a short time? Has he, perhaps, taken his cue from someone else? If so, who? Was it Meynert himself, who got all the credits in the introduction of Wernicke's dissertation? Of was it a certain Baginsky, who Wernicke mentioned in only one short sentence?*' Read Eling in a library near you and find out...

Ladies and Gentlemen, I could provide many more examples of Paul Eling's contributions to documenting the history of aphasiology in particular or of the neurosciences in general. But I'd much rather give the floor to Paul himself. The title of his lecture is *aphasiology: where and how?*



Aphasia: where and how

Paul Eling

Donders Institute for Brain, Cognition and Behavior
Radboud Universiteit Nijmegen

Introduction

A person may suddenly lose his capacity to express himself in speech or in writing, and he may also experience problems in understanding what is said to him or what has been written. These problems often occur as a result of brain damage, either due to, for instance, a problem with blood supply to the brain, a tumor or a traumatic injury. This phenomenon can be diagnosed as aphasia, a rather generic term. People have always suffered from this disorder, but the way the phenomenon has been interpreted and described in the period before the 17th century differed remarkably from how scholars looked at it in more recent times. In the 19th century the investigation of the brain formed a dominant issue for many scientists, in particular the notion that psychological functions might be localized in the brain, or more specifically, in specific areas in the brain. The study of aphasic patients was the primary ‘research-method’ for this issue. The debate aroused much interest and emotion. Even today, the localization discussion is still a central issue.

In this paper I will analyze the discussion on aphasia in the 19th century in the context of the localization question. Rather than focusing on the localization debate, I will try to address the following question: did these scientists have any idea what they were trying to localize, that is, how did they conceive of language when they were pointing to spots in the brain where they claimed it was localized? I will give a short description of the manner of thinking in the period before the 19th century. I will then describe the

positions of Gall, Broca, Baginsky, Wernicke and Steinthal with respect to their views on language and language disorders. Apart from Steinthal, these early aphasiologists conceived of language primarily as a process of relating a concept to a word. In case a general language function was assumed, its function was not clearly specified. Steinthal's view focused on the formulation of a proposition and the expression of the relation of a subject to an action, but his model was completely neglected among aphasiologists. I will argue that an important lesson to be learned is that one has to have a reasonably well established description of the cognitive function before one can attempt to localize it in the brain.

The beginnings

Wollock analyzed ideas on the physiology of speech in medical texts from Aristotle and Galen to the 17th-century, when Descartes came forth with his dualistic conceptions of body and mind. (1) Speech was considered a particular case of voicing, special to man. Emphasis was first on the bodily *instruments* that are required to make noise (lungs, air, larynx), second on *modulating* the noise to become speech sounds (vowels and consonants), and third on producing these sounds in *sequential order*. A number of disorders were distinguished, including: *traulotes*: reduced control over the production of certain speech sounds; *psellotes*: the absence of speech sounds or syllables in speech; and *ischophonia*: stuttering, i.e., incorrectly connecting a syllable to a subsequent syllable, lengthening a sound, or duplicating a syllable. Clearly, some aspects of aphasic speech may have been characterized with these terms, but current aphasiologists (or neuro-linguists) would not regard patients with such problems as aphasic. They would probably be classified as dysarthric. The specific problems with speech production that we would currently classify as aphasia, would probably have been regarded as a memory problem. Usually the mind was conceived of as consisting of, roughly, three components: perception, evaluation and memory and whatever we learn, including language, is stored in memory.

O'Neill identifies as a turning point the beginning of the 16th century. (2) Benton and Joynt reviewed 'Renaissance descriptions', to some extent similar to those discussed by O'Neill. (3) These works reflect a shift in

medicine during the 16th century to an analysis of mental functions in relation to the brain, a change presumably due to the fact that physicians started to perform their own anatomical observations, rather than relying on typically Galenic classical texts. The case descriptions may be best characterized as observations, usually not very systematic and usually not meant to illustrate a particular theoretical view of language or brain.

Johann Gesner's (1738-1801) elaborate case description, to be found in the chapter *Die Sprachamnesie*, in volume two of his *Sammlung von Beobachtungen aus der Arzneigelahrtheit* can be considered the first major work devoted to the subject of aphasia according to Benton. (4,5) The patient, 73-year old K.D., had been in excellent health but was unexpectedly affected by a severe language impairment. (6) His output was fluent but neologistic. K.D. could no longer read or write, and he had no sign of paralysis. He had been seen by several physicians, and Gesner described their observations and interpretations, referring to letters from these physicians. He concluded that the disorder cannot be ascribed to loss of intelligence, neither is it due to a generalized memory disorder, but rather it is due to a verbal memory impairment (consistent with Medieval cell doctrine; see Whitaker) (7). The nature of the impairment, Gesner specified, consists of an inability to associate images or abstract ideas to their expressive verbal symbols. Gesner's theoretical analysis is a first attempt to provide a functional explanation of aphasia, one that would become a central issue for discussion in the late-19th century. (5)

Localization of function

The 19th century witnessed a dramatic change in the investigation of mental processing and its relationship with the workings of the brain. The Austrian physician and anatomist Franz Joseph Gall (1757-1828) started the discussion, arguing that: 1) the material substance of the brain, in particular the cortex, forms the basis of mental functions (instead of the cavities inside), and 2) each mental faculty has its own seat, a circumscribed area of cortex (8,9). On the premise that focal changes in brain volume alter the shape of the overlying skull, an idea borrowed from the physiognomist Johann Christian Lavater (1741-1801), Gall looked for bumps on the skull to help him localize specific functions. Indeed, craniometry was his primary

method. He believed that studying the effects of lesions of various parts of the brain on language behavior, or the clinico-pathological method, could provide support for his cranium-based localizations, although he did not have great faith in clinical findings by themselves.

Gall

Gall (1822-1825) distinguished the language faculty (*Sprachsinn*) from the word faculty (*Wortsinn*), the former being an inborn capacity for (verbal) communication and the latter a store for words. (10) The language faculty was supposed to be highly developed in literary and philosophical men, while an individual could possess a large word memory without being very smart. Gall suggested that the organ of the memory of words was localized in what we now would refer to as the orbital gyrus, and the organ of the language sense was located on the mid portion of the supra-orbital plate. These ideas were based on Gall's observation of some of his class mates, who appeared to excel in languages on school but also had protruding eyes, as if these were pushed forward by that portion of the brain just behind the eyes. But Gall also recognized the specific effects of brain lesions on mental faculties as evidence for the localization of a given organ or faculty.

He described 6 cases, arguing that the observed language disorder is not due to general problems with intelligence or memory or to a paralysis of the tongue. With respect to one of these cases he drew the following conclusion: "he has only lost the capacity to speak". This is an interesting conclusion. We will see below that this 'capacity to speak' became an important component of the language process, but in fact Gall did not distinguish such a faculty, independent from word memory or the general language faculty. Perhaps he would not have considered such a capacity as a mental faculty. He clearly observed that there was free movement of the tongue so he would not have considered it to be a purely motoric problem. The problem was limited to speech and did not entail the production of sounds in general.

Gall's descriptions were not meant as a first step to understand how language is processed by the brain. Rather, they were just an example of the localization of mental faculties. However, the localization of language turned out to be the principal example for establishing the localization.

Broca

Bouillaud, a disciple of Gall, attempted repeatedly to promulgate this localization principle, from the 1820s to the 1850s, but he failed to convince the medical and scientific establishment. (11-13) Pierre Paul Broca (1824-1880), however, did change the prevailing view. (14) In the April 18th meeting of the Society of Anthropology in Paris, Broca mentioned in a discussion on disturbances of speech an important observation, according to the notes:

M. Broca presented the brain of a fifty-one-year-old man who had died [on the previous day] in his service at the hospital Bicêtre. For the last twenty-one years this man had lost the use of his speech. It is planned to deposit the specimen at the Musée Dupuytren and to publish the complete records in the *Bulletin de la Société Anatomique*.

The patient was a man called Leborgne, better known among aphasiologists as ‘Tan’. The full report was published in August. Broca stated that this patient could voluntarily utter the syllable “Tan” and occasionally few other small words, and that he had a lesion in the anterior part of the brain. (15,16) Broca indicated that this evidence supported the general claims of Gall, but that the lesion in his patient, at the foot of the third frontal gyrus, did not really match the site proposed by Gall.

There is no trace in his papers on aphasia to suggest that Broca was acquainted with linguistics. (17) The reader looks in vain for concepts like ‘grammar’ or ‘word formation’. What Broca described can, perhaps, best be referred to as a psychological model for language production. He distinguished three levels, on which functions or groups of functions operate. On the highest level ideas are developed (the general language faculty). On the second level that idea is mapped onto the conventional signs, the verbal forms of language. On this level different faculties operate. If one wants to express oneself in speech, the articulated language faculty will be called upon for this mapping function. If one prefers another mode of expression other faculties come into play. These two levels belong to the ‘intellectual’ part of the brain. He also considered these to be higher level functions because they are restricted to man. In the discussion which took place in 1863 Broca argues that animals, although deprived of speech, transmit their primitive ideas with signs that we do not comprehend but which he

considers to be a particular type of language. (In my view Broca is inconsistent here.) The last layer belongs to the motoric part of the brain. At this level the faculties governing the action of muscles and nerves for the actual emitting of the message are represented. Broca is only slightly more specific about each of these three levels.

The general language faculty is described as the faculty to establish a constant relation between an idea and a sign. This general faculty presides over all modes of expression. With respect to the second-level faculties, Broca claimed that the faculty is used to coordinate the movements for speech. One property or aspect of the faculty is a memory of procedures for articulating the words. It is not a memory of the words themselves, because the aphasic still knows the words and their values. This memory is independent of other memories and is also not a part of a general memory for movement. What is not clear in this description of the faculty is how it uses the memory to relate ideas to the conventional verbal forms. One could look at it as a retrieval mechanism: on the basis of conceptual information, the right procedure is retrieved and this is passed on to the third-level functions. Thus little interesting work is left for these third-level functions. They pull the strings according to the program they receive from the faculties they serve, as Broca expressed it.

After collecting a few additional cases, Broca claimed that a lesion in the third frontal gyrus results in *aphemie* (aphemia; derived from the Greek *phèmi*: I speak), a disturbance in the articulation of words – the mechanism for expressive, voluntary speech being impaired. (18) Armand Trousseau suggested the term *aphasie* (aphasia; derived from the Greek *phasis*: word) for the disorder. (19)

In 1865, Broca claimed that only the frontal gyrus in the *left* hemisphere was responsible for speech, thus not only further establishing the principle of localization, but also introducing the notion of hemispheric differences, very much to his own surprise. (20) The latter concept was quickly adopted in the literature and speech began to be interpreted in terms of cerebral dominance. (21)

While the notion of aphasia is currently regarded as a generic term, referring to a broad class of language disturbances, Broca referred to a specific disorder: a faculty to coordinate movements for speech. He recognized that language encompassed other components, but he did not speculate on what

would happen if one of these components would be disturbed. Neither did he refer to patients with disorders in other aspects of language behavior other than speech, such as reading or writing.

We now know that patients that can only produce one or a few words or syllables suffer from a very severe language disorder; they are usually classified as 'global aphasia' and not as 'Broca's aphasia'. Language production and perception are impaired. We now would probably not agree with Broca's interpretation of the nature of the deficit in his patient Leborgne. This shows that Broca's view on what actually the notion of language as a mental faculty implies, as well as his methodology to support his interpretation were very global.

Baginsky

Adolf Baginsky, who later specialized as a pediatrician in Berlin, rather early in his career wrote a paper on aphasia. (22,23) The paper is remarkable for two reasons.

First, he presented two patients suffering from aphasia due to renal failure. He indicated that in earlier papers a variety of etiologies had been described and he now wanted to argue that also renal problems may lead to aphasia. The description of the language deficits is very poor. Moreover, no systematic examination of the different language modalities was performed; apparently only phenomena observed during bedside examination are presented. Nevertheless, from his description it is clear that communication was very difficult, but these problems can probably be better interpreted as resulting from a general reduction of consciousness rather than a specific language problem.

A second, even more remarkable feature of this paper is that Baginsky formulated a theory of language processing as a framework for interpreting aphasic symptoms. Yet, there seems to be hardly any relationship between the nature of the language disorder in these two cases and his rather elaborated language model.

Baginsky argues that language is not an innate function but learned on the basis of experience.

The essence of human language, he argues, consists, generally speaking, of learning to associate particular objects to certain articulated sounds. In order to learn these associations between sounds, words and concepts, one needs different centres:

1. The centre for perception of sound, to which the normal end apparatus of the N. acusticus sends its sensations.
2. A centre capable of retaining certain received sound sensations, i.e. a centre for sound memories.
3. A main centre, to which the “memory centres” of all sensory nerves send their fibres. This centre can form concepts by connecting the separate sensory impressions. Certain sound forms, related to certain visual images call forth the image (“Vorstellung”) of particular objects. The “concept” of an object can only arise, if at least two sensory impressions, related to the same object and present simultaneously, connect to each other.
4. The main centre for the building of concepts is connected to a centre of co-ordinated movements.

His theoretical framework consisted of a series of specific language functions or centers, (e.g., for speech production and comprehension, concepts, reading and writing) that were connected to each other through “pathways”. These models are often referred to as connectionist models or diagrams. (24,25) Although the centers were often assumed to be localized in circumscribed brain areas, frequently these authors focused on the functional characteristics of their models. The typical structure of these models was that a language disorder occurs either by destruction of a center or disruption of a pathway. Adolf Kussmaul’s (1822-1902) comprehensive discussion of language phenomena in general, and of these wiring diagrams in particular, provides an excellent example of how such process models can explain aphasic behavior in a functional way. (26,27)

Figure 1. Diagram of Baginsky

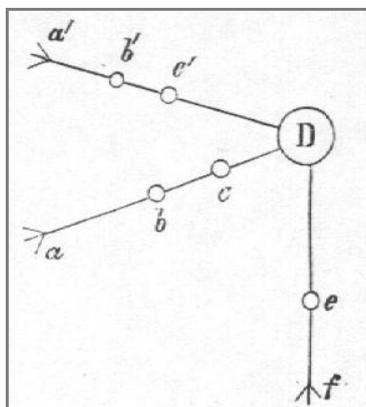


Figure Baginsky's model of language centres.

- a) are the endings of the N. acusticus
- b) is the centre for sound perception
- c) is the centre for sound memory
- D) is the centre for concept construction
- e) is the centre for co-ordinated movements
- a', b', and c' are the same organs in the visual pathway

From this model, one can infer different forms of language disorders.

He first distinguished two main categories, depending on whether the interruption is in the pathway from a to D or from D to e, the first he called a centripetal disorder, the latter a centrifugal disorder.

Language disorders resulting from sensory problems (e.g., deafness) or motor problems (articulation problems due to paresis) should not be regarded as aphasia. Aphasia results from damage to the centres b, c, D and e, and their connections. The phenomena will be different, depending on whether the one or the other is disrupted or whether the pathways are disconnected.

Assuming that c is disturbed by a severe pathological process, then the patient is in the situation of a deaf-mute child, with the difference that he can perceive sounds, while the child is missing this as well; the result is therefore the same for both, namely that the patient cannot speak, because he has lost every sound memory. He can, for instance, see a tree, he can

draw it, he can write the word “tree”, as long as the visual sense and touch sense have an intact connection with D; however, he cannot say “tree”.

The larger the lesion of the centre *c*, the more sound forms are missing, and the smaller the vocabulary of the patient will be. – Is the lesion of *c* relatively small, then it may occur that the patient has lost the sound memory of just a few sound forms, perhaps only of a few consonants; he may then utter words and drop every time those vowels and consonants. It must be kept in mind that for those forms of aphasia, that result from a lesion of the centre for sound memory, the patient is unaware of the missing of sound forms. The patient does not know that he cannot say particular sounds, or that he leaves out certain speech sounds; in this aspect these disorders differ from the ones that result from lesions of the centre *e*.

The (centrifugal) types of aphasia that result from destruction of *e* are characterised by the following. The concepts are not lacking; the sound memory is normal. The sounds correspond in the patient’s mind completely with what they usually mean in language; but the patient lacks the capacity to express his clear thought. These individuals are completely aware that they speak badly and this awareness, together with the sense of incapability to perform better, makes the patient tearful, apathetic, etc. The centrifugal forms of aphasia differ from the centripetal forms precisely in the awareness of the language disorder.

It remains to clarify the forms of aphasia, that result from lesions of the “concept centre D”. These are the real difficult but yet very frequent forms; in this condition thinking suffers as well as the language capacity. The “concepts” are missing. For this reason language disorders in these conditions are accompanied by disorders of the capacity to write.

We now may wonder why Baginsky’s model was not appreciated by other aphasiologists. Clearly, they may have had problems accepting Baginsky’s patients as real aphasics. And this might have been a reason to reject all his speculations on his language model and the different forms of aphasia derived from them. Later others did refer to his paper but only to note that Baginsky produced the first diagram. The idea of describing language as a set of centers with connection and deriving different forms of aphasia from that model has generally been ascribed to Wernicke. Wernicke knew Baginsky’s paper and mentioned, but immediately rejected his contribution as the model was not based on neuroanatomical data.

Wernicke

Carl Wernicke (1848-1905), at the relatively young age of 26 and without much experience with aphasic patients, wrote perhaps the most influential 19th-century monograph on aphasia, *Der Apahasische Symptomenkomplex*. (28-30)

Figure 2. Portrait of Wernicke



After his stay with Theodor Meynert in Vienna, where he performed neuro-anatomical analyses of the auditory nerve pathway, Wernicke studied 10 patients, and performed post-mortem analyses of the lesions in four of them. He noted that the clinical picture varied from pure motor aphasia to pure sensory aphasia (his terms). He claimed that in addition to a speech production area in the frontal lobe, speech perception is localized in the temporal lobe, in an area now known as Wernicke's area. These two centers are connected by nerve fibres. Lesions in either of these centers or in the connecting pathway would result in different patterns of language impairments.

Wernicke's ideas about language are similar to Baginsky's. Language refers to auditory word images, associated with representations of an object

from different sensory modalities. Wernicke contended that there was not a specific center for concepts, unlike Baginsky and some other late-19th-century authors thought. Concepts were, in his view, represented by sensory-motor representations and therefore represented over the entire cortex rather than in a centre.

Wernicke's model is an early attempt to provide a more detailed view of language as a psychological function, relating distinct components of that function to different sites in the brain. (31) However, keeping in mind that Wernicke formulated his model on the basis of patients with language disorders and not on a sophisticated view of language, it may be more appropriately regarded as a new theoretical account of aphasic phenomena. His approach became very influential, both in the domain of aphasia and in other functional domains, such as perception and motor control. His ideas were disseminated in the literature by a large number of pupils, including Liepmann, Heilbronner, Foerster, Kleist and Goldstein, among others.

What we now regard as the prototypical diagram was produced by Ludwig Lichtheim (1845-1928). It contained a separate center for concepts. (32,33) The model predicted seven different aphasia syndromes, but Lichtheim elaborated on only three types, motor and sensory aphasia, as well as conduction aphasia (*Leitungsaphasie* according to Wernicke); the latter due to a lesion of the pathway connecting the two centers. He illustrated the value of his model with 4 case descriptions (with pathological-anatomical data for one patient), claiming that each of the seven forms exists.

Steinthal

The above mentioned models on the representation of language in the brain were formulated by physicians, none of whom seemed to have a special training in linguistics. I will now discuss the ideas of a linguist, who may be considered the first psycholinguist. (34) In his *Introduction in the psychology and language science*, which is the literal translation of the subtitle of his book *Abriss der Sprachwissenschaft*, he first described his psycholinguistic theory. Subsequently, as a kind of proof of the usefulness of his theory, he applied it to language disorders, in order to show how it could explain features of aphasic speech.

As Steintal's views on language differ from what we have seen above, and as they are relatively complex, I will elaborate on these somewhat more. (35-37). The lowest level of language, he argues, is formed by an emotion-based representation of experiences or impressions ('Wahrnehmung'). At this level the utterance of sounds is a reflex action. With 'sound' Steintal means the sound representation of a word, which in infant speech may not be a regular word. The sound represents the 'totality', i.e., a person or animal or an object in action, in motion or following a movement. At this level the conceptualization of an object always contains an activity or a situation so that at the onset the mind has comprehensive images of events (processes, actions, 'Vorgänge'). For instance, the expression 'waf' of a child may refer to a barking dog. The onomatopoeic sound reflex is a sound sign because, and as long as, it represents entire perceptions and impressions. It becomes a word only when it signifies a single moment of an impression, an object or a feature. At the same time, this means that the close relationship between meaning and feelings is lost. The role of feelings now becomes increasingly weaker. Impressions can be evoked directly through the sound.

How does a human mind get from a 'word-less' stage to the level at which speech is produced in sentences? The development of real language requires social interaction. The major impetus underlying the development of speech is the desire to know what the other party does, where they are, or to communicate to a third party what the other is doing. An extremely important condition is the development of the notion of a person, an individual, or a subject. Perceiving people in action, with varying features, is a basis for this.

A child begins with understanding and imitating onomatopoeic expressions from adults: e.g. bow-wow. This bow-wow is neither a noun, nor a verb or adjective; it is not object, action or feature but it stands for everything the dog is and does. The entire meaning cluster, the interwoven mass of related impressions is represented in the child's consciousness. Soon the child finds out that there are more bow-wow's, and that his bow-wow can be in different positions or conditions, where bow-wow becomes a centre to which perceived differences and distinctions are attached. In this way, bow-wow becomes subject and the changing features the predicate.

These neurologists, so Steinthal argues, had distinguished three processes: the general centre for intelligence; the function of speech is governed by two independent centres: first, a centre steering the materialistic mechanism of articulation, that is, the motor or sound centre, and secondly, a centre for the psychic aspect of language.

There is no doubt about the function or the localization of the motor centre. It lies beneath the corpora quadrigemina and stretches from the pons to the olivaries. It contains the origin of all nerves that go to the muscles of the tongue, the palate, the larynx and the face (hypoglossus, vagus and facialis). Damage to this centre will result in *anarthria*. With respect to the second centre, the entire conceptualization is flawed in Steinthal's view. Damage to this centre was thought to result in aphasia. In an effort to find the exact site, the doctors neglected to observe, in detail, the psychological phenomena of the disorder.

We now get to the point where Steinthal explains different aphasic phenomena. Steinthal starts from the assumption that our mental possessions consist of several larger and smaller clusters of knowledge ('Erkenntnis-Gruppen') and judgements, which are each independent to a large extent, even when they are related to each other. According to the purely psychological theory, it is easy to understand that symbolic clusters are, in comparison to object clusters ('Sach-Gruppen'), more vulnerable and restore slower after damage. The reason being that all associations based on unnatural or artificial hyphens (and symbols belong to these) have less power and are more easily deranged than those based on objective relations. This also explains why proper names disappear from memory first, since they are related to a person or a place with an individual association. Steinthal also believed that from his exposition of the development of the sentence form it follows that verbs and adjectives are retained better than nouns. It is obvious that the word is much more important for the formulation of motion- (or activity-) images and qualitative images than it is for the images of objects, which are much closer to the impressions. One can have the image of an object without having the word for it, but a feature or an activity is mostly thought of in words, since they are abstract.

Having explained the language system in general, Steinthal turns to several pathological phenomena in order to provide a more detailed illustration of the language system. (38) First, he explains *stammering*, *stuttering*, and

anarthria. The latter condition is a permanent incapacity to utter words that the patient has in consciousness since he can write them. In this condition the speech organs are intact, however, either the motor centre for speech is affected or the pathway between this motor and the psychic centre for speech is inhibited, so that the commands of the latter are not executed. Steinthal defines all this within a single page, three years before the publication of Wernicke's book. Apparently, to him, this is all very clear and simple. The concepts for motor and psychic centres for speech are obviously concepts that do not require any further clarifications, just like the idea that there is a pathway between these two centres and that this connective pathway can be disrupted, leaving the centres intact and nevertheless resulting in a language disorder.

Finally, Steinthal describes several phenomena that fall under the notion of *aphasia*. Aphasia is commonly understood, Steinthal writes, as the acquired inhibition or abolishment of the inner word formation ('Wort-Bildung') caused by a deficit in the functioning of the psychic centre for speech without any affection of the articulation mechanism.

Steinthal says that different gradations of aphasia can easily be observed. First of all, there can be a complete absence of words ('Wortmangel'). Steinthal regards the cases with pure aphasia of more interest where particular word groups are affected. In these cases the words that represent certain images simply do not come forward, although they are at the patient's disposition. The categories that usually are lost are nouns, in particular names, while verbs and other word classes remain available. Speech is fluent and the patient may even be talkative ('red-selig')! We would refer to this as Anomia or Amnesic Aphasia. An even higher grade of aphasia is present when the patient no longer understands words. A general lack of understanding of symbols is described as *asemia*; a disorder described by Finkelnburg in 1870 in Berlin.

However, Steinthal not only points to (systematic) differences in degree of aphasia. He also believes that there are important differences in the nature of the deficit that makes a principled distinction warranted.

First, aphasia may occur primarily in the form in which the reproduction of the word form is impossible. The problem lies in the activation of the word form (the string of sounds). The patient may produce the wrong words, but he is aware of erring. In a second form the patient does not notice mistakes,

but believes he has used the right word; in this case judgment is affected. Judgment implies comparison, and this is, as with relations in general, not possible without sufficient 'reproduction power'. Patients may echo words, persevere, and use words that are associated to words heard. Usually, in this form of aphasia the patient will understand what has been said. Sometimes, however, the reproduction capacity for sound forms is so weakened that the patient cannot comprehend.

Third, at first this lack of judgement and freedom extends over words as mere sound forms. However, the sound forms are associated to an image causing a more serious language capacity disorder, in which the patient is incapable of reproducing not only the sound form but also the image itself. In this case the speech process itself, whereby the function of transforming a concept into an image occurs, i.e. the sentence formation, is inhibited. These two levels (mentioned in the first and third point) should be distinguished. This distinction between the two forms seems to be so important to Steinthal that he suggests to name the first *aphasia* and the second *akataphasia*.

This distinction can also be formulated in another way. Language as a psychic mechanism consists on the one hand of an immense number of images An (subjects) and Nn (predicates); on the other hand there are methods (laws, rules) and means (particles, forms) to connect these images in order to form sentences. Accordingly, apart from expressing the meaning, the correct construction of sentences is a purpose of language, indeed its second purpose. It is of course, as a means, subordinate to the content, but, nevertheless, something that has to be achieved in itself. Whenever it happens that the mechanism of consciousness does not produce the An (e.g., mother) and Nn (e.g., walking) necessary for representing the content, *aphasia* occurs. However, it is also possible that the power is lacking to apperceive, or connect, the images according to the grammatical laws: this we call *akataphasia*.

What did they localize?

I have described some ideas on the effects of brain lesions on the language capacity, as formulated by a few men in the 19th century, interested in a specific form of language disorder namely aphasia. Some of them, Gall,

Broca and Wernicke were generally recognized as central figures in the discussion on the relation between language and the brain. Two others, Baginsky and Steinthal were less well known, at least among aphasiologists. The discussion on aphasia was primarily a discussion on the validity of the concept of localization of function, as formulated by Gall at the beginning of that century. I have described the views of these men on language. Broca recognized that language was much more than the classical memory store for words. He argued that there are different levels of language processing and within levels different modalities may be discriminated. However, his model of language processing was obviously pure speculation and not supported by empirical evidence. He only provided some empirical findings that allowed him to argue that the faculty of articulating words is localized in the frontal lobe. Baginsky and Wernicke stressed that language is learned and is based on senso-motor experiences. Objects are seen, words are heard and the various images or representations become associated. There is some specialization within the brain for storing images of a particular modality in a particular area. Thus, various centres develop. Baginsky and Wernicke distinguish between a word form and the conceptual representation, which is supposed to consist of the integrated connection of different representations of an object. Accordingly, a concept is also of a senso-motoric nature, not abstract. Baginsky and Wernicke do not recognize a general language faculty. Steinthal started from a rather different conception of language: language is a means to express an integrated message. He argues that an object is never seen as an isolated object, but it is always seen in a particular mode and context. This integrated representation is analysed, apperceived, in its constituting parts and thus reveals a subject and a predicate. This is the basis of sentence production. In this respect Steinthal's view is essentially different from what the physicians claimed. And in my view, Steinthal points to an essential feature of language: the expression and understanding of a message or communication.

These differences in views on what essentially language is, will have important implications for localizing language or language components. And if one wants to look for brain areas involved in language behaviour, it is important to have a reasonable idea of what language actually is. It is remarkable to see that Broca and Wernicke hardly bothered to explain what

language actually is, and provided no evidence in favour of their language model (independent from the aphasic symptoms). In contrast, Baginsky did elaborate on a model of language behaviour and derived aphasic symptoms from that. But even he did not indicate on what evidence his language model was based. Steinthal himself also did not provide empirical support for his model, but it was formulated within the widely accepted psychology of Herbart. In that sense, his model did fit in a recognized framework for understanding mental functions like language. Nevertheless, this history of aphasia may teach us a lesson to formulate a clear and valid view of how a mental function works before we start to search where in the brain it is localized.

References

- [1] Wollock J (1997). The Noblest Animate Motion Speech, physiology and medicine in pre-Cartesian linguistic thought. Amsterdam: Benjamins
- [2] O'Neill YV (1980). Speech and Speech Disorders in Western Thought before 1600. London: Greenwood Press.
- [3] Benton A, Joynt RJ (1960). Early descriptions of aphasia. *Arch Neur*, 3, 205-222.
- [4] Gesner JAP (1770). *Sammlung von Beobachtungen aus der Arzneygelahrtheit*. Zweyter Band. Neue verbesserte Auflage. Nordlingen: Beck.
- [5] Luzzatti C (2002). Johann August Philipp Gesner (1738-1801). A review of his essay "The language amnesia" in the bicentennial anniversary of his death. *J Hist Neurosci*, 11, 29-34.
- [6] Benton A (1965). Johann A. P. Gesner on aphasia. *Med Hist*, 1, 54-60.
- [7] Whitaker HA (2007). Another look at medieval cell doctrine In: H. Cohen and B. Stemmer (Eds.) *Fragments of the Mind and Brain*. London: Elsevier Science.
- [8] Lesky E (1979). Franz Joseph Gall. *Naturforscher und Anthropologe*. Bern: Huber.
- [9] Finger S (2000). *Minds Behind the Brain: A History of the Pioneers and Their Discoveries*. New York: Oxford University Press.
- [10] Brown J, Chodor K (1992) Phrenological studies of aphasia before Broca: Broca's aphasia or Gall's aphasia? *Brain and Lang*, 43, 475-486
- [11] Bouillaud J-B (1830). Recherches experimentales sur les fonctions du cerveau (lobes cerebraux) en general, et sur celles de sa portion antérieure en particulier. *J Hebd Méd (Paris)*, 6, 527-570.
- [12] Bouillaud J-B (1848). Recherches cliniques propres à démontrer que le sens du langage articulé et le principe coordinateur des mouvements de la parole résident dans les lobules antérieurs du cerveau. *Bull l'Acad royal Méd*, 1^{er} trimestre, 699-719.

- [13] Luzzatti C, Whitaker H (2001). Jean-Baptiste Bouillaud, Claude-François Lallemand and the role of the frontal lobe: location and mislocation of language in the early 19th century. *Archiv Neur*, 58, 1157-1162.
- [14] Schiller F (1992). Paul Broca, Founder of French Anthropology, Explorer of the Brain. New York: Oxford University Press.
- [15] Broca P (1861). Perte de la parole, ramollissement chronique de destruction partielle du lobe antérieur gauche du cerveau. *Bull Soc d'Anthrop Paris*, 1861 (seance du 18 avril), 235-238.
- [16] Signoret J-L, Castaigne P, Lhermitte F, Abelanet R, Lavorel P (1984). Rediscovery of Leborgne's brain: Anatomical description with CT Scan. *Brain Lang*, 22, 303-319.
- [17] Eling P Paul Broca (1824-1880). In: P. Eling (ed) *Reader in the history of aphasia*, Amsterdam: Benjamins
- [18] Broca P (1863). Localisation des fonctions cérébrales. Siège du langage articulé. *Bull Soc Anthropol Paris*, 1863 (seance du 2 avril), 200-204.
- [19] Trousseau A (1864). De l'aphasie, maladie decrite récemment sous le nom impropre d'aphémie. *Gaz Hop civ milit*, 37, 13-14, 25-26, 37-39, 48-50.
- [20] Eling P (1984). Broca on the relation between handedness and cerebral speech dominance. *Brain Lang*, 22, 158-159.
- [21] Harris LJ (1991). Cerebral control for speech in right-handers and left-handers: an analysis of the views of Paul Broca, his contemporaries, and his successors. *Brain Lang*, 40, 1-50.
- [22] Baginsky A (1871). Aphasie in Folge schwerer Nierenerkrankungen.-Uraemie. *Berl Klin Wochenschr*, 8, 428-431; 439-443.
- [23] Eling P (2005). Baginsky on Aphasia. *J Neuroling*, 18, 301-315.
- [24] Moutier F (1908). *L'aphasie de Broca*. Paris: Steinthal.
- [25] Morton J (1984). Brain-based and non-brain-based models of language. In D. Caplan, A. R. Lecours, & A. Smith (Eds.), *Biological perspectives on language*. Cambridge: MIT Press.
- [26] Kussmaul A (1877). *Die Störungen der Sprache. Versuch einer Pathologie der Sprache*. Leipzig: Vogel.
- [27] Jarema, G. (1993) *In sensu non in situ: The prodromic cognitivism of Kussmaul*. *Brain and Language*, 45, 495-510.
- [28] Wernicke C (1874). *Der Aphasische Symptomencomplex. Eine psychologische Studie auf anatomischer Basis*. Breslau: Cohn & Weigert.
- [29] Eggert GH (1977). *Wernicke's Works on Aphasia: A Sourcebook and Review*. The Hague: Mouton.
- [30] Tesak J (2005). *Der aphasische Symptomencomplex von Carl Wernicke*. Idstein: Schulz-Kirchner Verlag.
- [31] Geschwind N (1966). Carl Wernicke, the Breslau school and the history of aphasia. In: Carterette, E. (ed.) (1966) *Brain Function*. Berkeley: University of California Press.
- [32] Lichtheim L (1885). Ueber Aphasie. Aus der medicinischen Klinik in Bern. *Dtsch Arch Klin Med*, 36, 204-268.

- [33] Laubstein AS (1993). Inconsistency and ambiguity in Lichtheim's model. *Brain and Lang*, 45, 588-603.
- [34] Eling P (2006a). The psycholinguistic approach to aphasia of Chajim Steinthal. *Aphasiol*, 20, 1072-1084.
- [35] Bumann, W. (1965) *Die Sprachtheorie Heymann Steinthals*. Meisenheim an Glan: Anton Hain.
- [36] Christy, T. Craig (1987) Steinthal and the development of linguistic science: the convergence of psychology and linguistics. In H. Aarsleff, L.G. Kelly & H.J. Niederehe (eds) *Papers in the history of linguistics*. Amsterdam: Benjamins.
- [37] Christy, T. Craig (1989) Reflex sounds and the experiential manifold: Steinthal on the origin of language. In: J. Gessinger & W. von Rahden (eds) *Theorien vom Ursprung der Sprache*. Berlin: Walter de Gruyter.
- [38] Steinthal, H. (1871) *Abriss der Sprachwissenschaften*. Berlin: Harrwitz und Gossmann.

Laudatio Maurice Lamy

Eric Mortier

Maurice Lamy is the former chair of the Department of Anaesthesia and Critical Care of the University of Liège, Belgium.

During his rich career he has published over 300 scholarly articles covering a broad range of physiological, pathophysiological and pharmacological subjects.

He has witnessed the birth, the development and first clinical trials of artificial oxygen carriers.

He has contributed in this field of research by highly original scientific work.

Therefore it seemed fitting to the Sarton Committee to honour Maurice Lamy with a Sarton Medal as a “living historian” of a field of research that has not yet reached full maturity and still holds unfulfilled promises.

Current status of oxygen carriers

M. Lamy, G. Deby Dupont

Heavy medical interventions in severely injured patients and complex transplantation surgery are currently performed with success, but they have increased the need of human blood. At the same time, the risk of transmission of viral diseases, the risk of errors in blood transfusion and the insufficiency of palliative treatments (blood predonation, pre- and perioperative hemodilution, perioperative blood sparing, lowering of transfusion trigger) accelerated the development of blood substitutes as alternatives to human blood.

Together with the property of carrying O₂, a blood substitute must have at least the following properties:

- free of toxicity and side effects
- adequate O₂ uptake in the lungs and adequate delivery to tissues
- sufficient half-life time in the circulation to avoid repeated administrations
- harmful and rapid excretion
- stable at room temperature, easy to store and easy to use
- easy to sterilize (to assure the absence of pathogens and viruses transmission)
- cheap to manufacture.

Intense efforts in the field of blood substitutes started up and were largely supported since 1980s by investment of the US military, which was concerned by the need of a reliable resuscitation solution that could be used immediately after injury and did not need special storage conditions. Two majors approaches were developped and are still in clinical trials: the perfluorocarbon emulsions and the solutions of free haemoglobin [1, 2, 3].

1. Perfluorocarbon emulsions

The perfluorocarbons (PFC) are synthetic cyclic or linear hydrocarbons occasionally containing oxygen or nitrogen atoms, and in which the hydrogen atoms are replaced by fluorine atoms. These solvents were produced and used for their chemical inertia in the Manhattan project during World War II. They easily solubilize and release gases without interacting with them. The quantity of gas dissolved is linearly related to its partial pressure. Perfluorocarbons are dense transparent liquids, immiscible in water.

After the famous demonstration by Clark and Golan [4] in 1966 that an animal immersed in an O₂ saturated solution of perfluorocarbon breathed normally, the perfluorocarbons were soon considered as possible red blood cells substitutes [5]. But, because the PFC are dense and not hydrosoluble, they must be emulsified for administration in the intravascular space. The properties of PFC emulsions depend on the components of the emulsion (necessary presence of surfactants), on the proportion of the various components and on the size of the emulsion particles, which influences the stability of the emulsion, the surface area available for gas exchange, the viscosity, and the intravascular half-life (linked to *in vivo* toxicity or side effects).

First generation PFC emulsions

PFC emulsions were prepared as soon as 1967 with plasma, but were not used in humans. The first generation PFC emulsion for administration to human was Fluosol-DA[®], a 20% w/v solution developed by the Green Cross Corporation (Osaka, Japan). The product was made up of 2 PFC with a mixture of Pluronic F-68, egg-yolk phospholipids and glycerol as emulsifying agent [6]. It transported and delivered O₂ without major toxicity, but presented disadvantages: long tissue retention of one of its PFC components, low concentration of PFC and limited intravascular half-life both limiting the amount of transported O₂, and unsatisfactory stability. Fluosol also presented side effects, such as inhibition of white blood cells and complement activation, attributed to Pluronic [7].

Fluosol was used with success in around 300 patients who refused blood transfusion for religious reasons [8,9], and was authorized by the FDA for injection in humans (for percutaneous transluminal coronary angioplasty, PTCA). But the manufacturer stopped the preparation of Fluosol-DA for insufficient clinical use.

Second generation PFC emulsions

In the second generation emulsions, the PFC concentration is largely increased, enhancing so the O₂-carrying capacity and eliminating the dilution of patient's blood at time of administration. These emulsions are formulated "ready-for-use" in buffered saline, and present a high stability (resistance to heat sterilisation and to storage at + 4°C), due to the use of a crucial amount of egg yolk phospholipids and better emulsification techniques (high-pressure homogenization, microfluidization) [10]. The small size of their particles (mean diameter: 0.2 µm, about 1/35 of erythrocyte) allows them to easily maintain perfusion of all the capillaries of the microcirculation during states of local vasoconstriction and ischemia, when erythrocytes no longer circulate [11]. The archetypal second generation emulsion is Oxygent™ (Alliance Pharmaceutical Corp., San Diego, CA), 60% w/v PFC emulsion based on the use of a linear PFC, perflubron (perfluorooctyl bromide), with particles with a mean diameter of 0.16 to 0.18 µm. This emulsion dissolves 28 ml O₂/100 g at 37°C and 750 mmHg. It can be stored at refrigerated temperature for up to two years. The presence of the terminal bromine atom lends lipophilicity to perflubron and a more rapid excretion as vapors by the lungs, limiting its persistence in tissues. Its administration is not associated with hemodynamic effects and does not activate complement, but could produce a dose-dependent and transient flu-like syndrome four to six hours after infusion, which results from the phagocytosis of the emulsion particles by macrophages.

Numerous studies were performed in humans, particularly with Oxygent™, enrolling more than 500 subjects in phases I and II. An important clinical application of Oxygent™ is its administration during surgery with acute normovolemic haemodilution (ANH), to allow reductions of the patient's hematocrit below currently accepted thresholds while main-

taining or improving tissue oxygenation. In a phase II study in orthopedic surgery with ANH, the use of Oxygent allows the reversal of trigger for transfusion.

Phase III studies with ANH in cardiopulmonary bypass surgery and in high-blood loss non cardiac surgery showed a greater avoidance of transfusion, but were stopped for more serious adverse events in the PFC group, results which remain debated [12]. A new phase II clinical trial in major surgery was planned in France for the end of 2006, but financial problems arrested the study.

In November 2007, phase II clinical trials in major surgery were announced in China, with the purpose to maintain haemodynamic stability and improve post-operative organ function. At the beginning of 2008, the manufacturing technology of Oxygent was transferred to Double-Crane Pharmaceuticals Co. in China, and a pilot production started. In Russia, another PFC emulsion, Perftoran, similar to Fluosol, but with improved emulsifier and low size particles (0.07 μm) is still in clinical trials with success in improving haemodynamics, and in reducing ischaemic damage and allogeneic blood transfusion [13,14]. Out of Russia, Perftoran was used in valvuloplasty surgery with ANH [15].

Advantages and inconveniences of the PFC emulsions

The advantages of PFC emulsions as blood substitute are summarized in table 1: absence of incompatibility and risk of transmission of infectious diseases, long duration of conservation, easy access, absence of metabolism and more particularly no reaction and no binding with O_2 allowing easy tissue unloading, viscosity and rheologic parameters similar to those of blood, permitting the particles to flow through swollen and/or blocked capillaries, where red blood cells might not pass. The solubility of O_2 in PFC emulsions is proportional to the partial pressure, and the O_2 transport capacity of these emulsions depends on the PFC concentration. Emulsions containing 45 to 60% PFC (weight/volume) seem ideal in terms of O_2 carriage, but the mechanisms of transport and delivery are entirely different from those of erythrocytes. The saturation curve for erythrocytes is sigmoid, and a fall in partial pressure from 150 to 50 mmHg leads to unloading of 25 % of the bound O_2 . To obtain an efficiency in O_2 delivery

similar to that of oxyhemoglobin, an O₂ enriched atmosphere must be used [16], and 100 % O₂ are administered to patients receiving PFC emulsions. PFC are thus only O₂ carriers with a transport capacity greater than that of blood under hyperoxic conditions and a facilitated unloading of O₂ in the tissues. Side effects of PFC emulsions such as complement and phagocytic cells activation, principally due to the surfactant, are no longer seen with the second generation emulsions using newer surfactants. A liposome effect (coalescence of emulsion particles) was described, increasing the risk of stroke, but the question remains debated. At the opposite, beneficial anti-inflammatory effects were reported [17]. However, PFC emulsions still have a limited intravascular persistence, and there is a limitation to their use consecutive to the elimination of the emulsion particles by the reticulo-endothelial system [18]: large doses could lead to hepatic engorgement and a temporary impairment of immune defense mechanisms, a risk decreased by the small particle size of the second generation emulsions. The search for PFC in various tissues (lung, liver, spleen ...) showed neither high levels of accumulation nor excessive persistence, and there are no reported toxic or side effects that could result from oxidation of the phospholipidic surfactant or from in vivo production of lysophosphatides. PFC emulsions thus remain valuable candidates as oxygen carriers.

2. Haemoglobin solutions

The first transfusion of blood occurred in 1667 when the physician of the French king Louis XIV, Jean Baptiste Denis de Commercy injected 300 g of sheep blood to a young man: the assay was a success, but the physician observed emission of black urine by his young patient. Jean Denis de Commercy repeated the assay, but in 1668, a patient died after 3 “transfusions”, what led to the interdiction of blood transfusion. In 1818, James Blundell restarted human blood transfusion in several young women suffering at post-partum haemorrhage; Blundell is now considered as the “father of blood transfusion”.

- **Lysed erythrocytes: the first solution used to replace blood**

The first administration of a haemoglobin (Hb) solution obtained from the lysis of erythrocytes did not occur before 1898 when Von Stark [19] administered a Hb solution to patients in an attempt to treat anaemia. Rapidly, it appeared that free Hb was harmful, leading to disseminated intravascular coagulation, cardiac failure and renal toxicity. These observations and the chemical instability of Hb solutions led that line of research to be abandoned. In 1916, small quantities of free Hb were infused to human by Sellards and Minot, in order to study the clearance by the kidneys, and demonstrated signs of renal toxicity [20]. In 1937 a systemic and pulmonary vasopressor effect was described by Amberson in animals infused with lysed red blood cells, and this effect was not due to the simple expansion of circulating volume [21]. In 1949, Amberson infused 300 mL of a 6% Hb solution as a last resort to resuscitate a young woman suffering from a severe postpartum haemorrhage unresponsive to infusion of crystalloid, colloid, and homologous blood. This infusion increased the blood pressure and was associated with improved level of consciousness, what suggested that this pressor effect was beneficial [22]. Rabiner et al [23] further treated hemorrhagic shock patients with 180 to 300 mg/kg “stroma-free” hemoglobin, and Savitsky et al [24] administered 250 ml of Hb solution to volunteers with minor side effects on kidneys and cardiovascular system (first phase I clinical trial).

- **Modified haemoglobin solutions: source of free Hb and chemical modifications**

The major problems encountered during the early studies with free Hb were vasomotor effects, activation of the complement, kinin and coagulation systems, nephrotoxicity, interference with macrophage function, antigenic effects, histamine release, and iron deposits: they were attributed to erythrocyte membrane remnants. The renal toxicity was due essentially to the rapid breaking of the Hb molecule into its α , β dimers. Free Hb also presents an excessive affinity for oxygen (P50: 12-14 mm Hg) attributed to the absence of the allosteric effector 2,3 diphosphoglycerate (2,3-DPG). Purification of Hb from different animal species began in 1970, produced “*stroma free haemoglobin*” (SFH) and eliminated acute toxic effects of the free molecule. Chemical modifications of

the Hb molecule were designed to suppress the rapid rupture of the tetrameric molecule into its dimers and to avoid or reduce renal toxicity.

Chemical modifications of Hb molecule

The modifications which have been tried [25,26] are summarized in figure 4 [27]:

- internal stabilization of the α - α or β - β dimers by a cross-linking with polyanionic molecules (acetylation), bis-pyridoxal-5-phosphate (pyridoxylation) or dialdehydes derived from the oxidation of the cyclic structure of sugar (o-raffinose) or open ring-adenosine triphosphate (o-ATP),
- conjugation with large molecules (surface modification) with macromolecules [hydroxy-ethyl starch, polyethyleneglycol (PEG), Dextran 20] or artificial support (“nanocrystalline” beads),
- intermolecular cross-linking (polymerization) with cyanate or glutaraldehyde reagents,
- encapsulation in synthetic liposomes with co-encapsulation of other compounds such as antioxidant systems and enzymes to protect Hb from oxidation.

The modifications aim at increasing the stability and modifying the surface electric charges of Hb, in order to reduce its extravasation and increase its plasma half-life. Conjugated and polymerized Hbs have molecular weight ranging from 64,000 to 400,000 daltons and correctly deliver O₂ to tissues even when infused at low doses. The encapsulation and co-encapsulation techniques attenuate the vasoactive effects, and yield a P50 of 30 mm Hg, with a convenient kinetics of O₂ binding and delivery, but Hb liposomes have a short circulation time due to a rapid phagocytosis, with hepatic overload in relation with the infused volume.

Sources of Hb molecule

The sources of Hb are mainly human erythrocytes from outdated banked blood and bovine erythrocytes from slaughtered animal blood, both carefully purified. Free human Hb has an increased affinity for O₂ (P50: 12-14 mm Hg) compared to intracellular Hb, because it lacks the allosteric inhib-

itor 2,3-DPG [28]. Human Hb solutions have a high colloid oncotic pressure, limiting Hb concentration to 7 g/dL; they are stored in an anaerobic environment to avoid the oxidation into metHb. The bovine source is interesting for easy and cheap access, and because bovine free Hb does not require 2,3-DPG to control its affinity for O₂ and has a P50 of approximately 30 mm Hg, favouring O₂ delivery to the tissues.

Recombinant human Hb was produced in *Escherichia coli*, with the 2 α chains fused to avoid dissociation in plasma [29] or with a mutation on β chains (“Presbyterian” Hb) resulting in changes in the allosteric control mechanism and a lower affinity for O₂ [30]. This Hb variant (Optro®, Somatogen) has a P50 higher (30-33 mm Hg) than the natural Hb with an improved O₂ delivery and a plasma half-life 4 times greater than free Hb. Attempts were also made to produce recombinant Hb in yeast and transgenic plants and in transgenic animals (pigs, mice). But techniques of isolation and purification of the Hb molecule, and the scaling up of the production are still to improve.

• Clinical use of modified Hb solutions

Several companies developed free Hb solutions (table 3), which reached phase II and III clinical trials, but these solutions cannot replace the red blood cells in all their functions, since numerous components which are included in the red blood cell are lost during Hb purification. The Hb solutions have the primarily function of carrying O₂ to tissues. It is thus more accurate to design them by the terms “cell-free oxygen carriers”, “Hb-based oxygen carriers (HBOCs)” or “oxygen therapeutics”. They have also the function of restoring adequate volume in a large range of clinical situations with important blood loss such as cardiac surgery [31] and trauma [32]. All HBOCs have a short intravascular life-time and carry many side effects, with variable consequences (table 4). Therefore, several manufacturers stopped the clinical trials and the production of HBOCs.

Among all the HBOCs which reached the phase of clinical trials, two generations can be distinguished, the second generation of HBOCs being developed on the basis of the observations collected from the studies performed with the first one, which pointed out vasoconstriction and the gastro-intestinal symptoms.

First generation of Hb solutions

HemAssist™ (DCLHb; Baxter Healthcare Corp.) reached phase II and III clinical trials in orthopedic surgery, abdominal aortic repair surgery, major abdominal surgery and cardiac surgery. Modest results were obtained in allogeneic blood cell transfusion avoidance, and increased adverse events (hypertension, yellowing of the skin, haemoglobinuria and pancreatic suffering) and short plasma persistence of DCLHb (\pm 24h) did not support the routine use for transfusion avoidance [31,33]. A phase III clinical study in non-cardiac surgery was stopped early for safety concerns [34]. In trauma patients with severe haemorrhagic shock, a European “On-scene” multicentre study was prematurely arrested for lack of efficacy (mortality not significantly different in the treated group) versus the standard treatment group [35]. In a similar phase III study in patients with severe traumatic haemorrhagic shock in the USA, an increased mortality was observed [36], and subsequently, ongoing clinical trials were arrested and Baxter stopped the development of DCLHb.

For the recombinant Hb (Optro®, Somatogen Inc.), the phase II clinical study was stopped for hypertension, pyrogenicity and other adverse events [37,38]. Hemolink® (Hemosol Inc.) reached phase II and III clinical trials in high-blood-loss surgery a few years ago, but the trials were discontinued for safety problems [39], and the production of Hemolink has been terminated [40]. Encapsulated Hb in lipid vesicles were tried with success in preclinical animal studies, but there are no ongoing clinical trials with these products.

Two HBOCs are still in advanced clinical development: Hemopure® (HBOC-201) and PolyHeme®. Hemopure® was used in a phase III orthopedic surgery study, with doses ranging from 65g (\pm 1 RBC unit) to 325g (\pm 10 RBC units). A reduction of the need for allogeneic transfusion was observed, but with more adverse and serious adverse effects: gastro-intestinal events, elevated plasma levels of amylase and lipase and clearly hypertensive properties mainly in elderly patients [41,42] (table 4). Hemopure® is approved for sale in South Africa to treat acutely anemic surgical patients. A veterinary product, Oxyglobin® (HBOC-301) has been approved and is used in U.S.A. and Europe for the treatment of anemia in

dogs. The company announced that new phase II trials are being designed, but at the end of 2006, Hemopure® was still not approved by the FDA.

In phase III clinical trials (trauma and emergency surgery for aneurysm rupture), PolyHeme® up to 1,000 g in 10 L was administered with success: 50 % reduction of blood transfusion, no major concerns [43,44]. The study was halted late 2001, before completion. In the beginning of 2006, an online article of the Wall Street Journal revealed that adverse events (heart attack) were more frequent in the patients receiving PolyHeme®, but the company attributed these adverse events to an excess of total fluids given to PolyHeme® patients, and not to the product itself [45].

A multicenter phase III non-consent trial in trauma patients with severe blood loss started in January 2004 and the patient enrolment was completed in July 2006. The results published in the beginning of 2009 indicated a blood transfusion avoidance in the PolyHeme group with no difference in survival at 30 days, but higher adverse events (coagulopathy, hyperkern- sion, myocardial infarction) compared to the control group [46,47].

Second generation HBOCs: oxygen therapeutics

As it was suggested that hypertension observed with HBOCs was the consequence of NO trapping and of an arteriolar vasoconstriction in response to O₂ delivery [48], the group of Winslow [49] designed a new Hb molecule (MP4) by increasing the molecular volume of human Hb with polyethylene glycol, the affinity for O₂, the viscosity and the oncotic pressure. Animal studies showed that MP4 was safe and without haemody- namics effects.

For clinical use, MP4 (Hemospan®, Sangart Inc.) was designed as an O₂- carrying plasma expander administered at low concentration to deliver O₂ to hypoxic tissues; it is as an “oxygen therapeutics” more than a blood substitute. In phase II clinical studies [50,51], no serious adverse events could be attributed to Hemospan, and no significant hypertension was observed, but spinal anaesthesia by its hypotensive effect could have masked the hypertensive effect of Hemospan®. From these phase II studies, Hemospan® appears safe, but the doses are low (around 42g for the highest one), and despite these low doses, bradycardia and elevation of

hepatic and pancreatic enzymes are observed (this was also observed with the first generation blood substitutes). Questions remain concerning the half-time life of Hemospan® in plasma (around 20h) and the metHb production, so that studies with larger doses are expected before the innocuity (and the utility) of this new generation blood substitute can be firmly assured. Two phase III studies with Hemospan for prevention or treatment of perioperative hypotension in patients undergoing primary hip arthroplasty with spinal anaesthesia were recently completed in Europe: the publications of the detailed results are expected.

- **A meta-analysis: the death blow for Hb-based blood substitutes?**

A recent meta-analysis was performed on 16 randomized controlled trials involving 3711 surgical, stroke and trauma patients, with 5 haemoglobin-based blood substitutes (HemAssist, Hemopure, Hemolink, Polyheme and Hemospan) [52], used as outcome variables the data on deaths and myocardial infarctions, and demonstrated a statistically significant increase in the risk of death and the risk of myocardial infarction in the group treated with Hb-based blood substitute. From this meta-analysis and taking into account the well-demonstrated toxicity of haemoglobin out of the erythrocyte (particularly its ability to cross the endothelial barrier, to produce oxidant species, and to induce renal toxicity) [53,54,55], the use of HBOCs cannot be recommended especially in fragile (elderly and severe haemorrhagic) patients. Hope remains for Hemospan, but it is an oxygen therapeutics and not a substitute of RBC [48].

Conclusion and perspectives

Two PFC emulsions, Oxygent and Perftoran are still in clinical trials in China and Russia, with promising results in the treatment of local ischaemia and encouraging results in cardiac surgery with ANH. PFC emulsions remain thus probably valuable candidates as oxygen carriers. The HBOCs of the first generation have been used with moderate success in avoiding red blood cell transfusion, no significant results in improving survival, a short intravascular lifetime and an increase of severe side effects (hypertension, renal toxicity) compared to classical treatment. Hemopure® and PolyHeme® are the two HBOCs which remain in phase III clinical

trials, but with a questionable lack of published results. Hemospan® is still in clinical trial, but is more an oxygen therapeutics than an universal blood substitute.

A recent, perhaps promising approach is to encapsulate Hb in biodegradable nanocapsules of polylactide, which are degraded in vivo into water and carbon dioxide [56], contain around 11 g bovine Hb/dL and have O₂ carrying and delivery properties similar to that of free bovine Hb. The enzyme of the red blood cells can be co-encapsulated to protect Hb from oxidation into MetHb. However, this approach is still limited to animal studies.

Projects are on the way to obtain human Hb from micro-organisms (*Escherichia coli* and *Aspergillus niger*) or from worms, which have a polymeric Hb molecule, thus not needing chemical modification for sufficient stability in bloodstream. Successful preclinical assays seem to have been made, but technical problems of extraction remain to be solved, and there is no knowledge on the effects of worm Hb on blood pressure and on its sensibility to oxidation [3].

As a substitute for universal use blood remains necessary for urgent transfusion at the site of severe traumatic injuries, it is important to carry out more basic research for solving the problem of free Hb toxicity by oxidation and metHb formation. The most promising way remains the *in vitro* erythroid cell generation, for which important progress has been made: starting from human hematopoietic stem cells, conditions have been established for producing mature red blood cells after around 18 days of culture [57,58], but among the numerous problems which remain to be solved, the technical conditions for large scale cultures in bioreactors [59] and the control of the membrane expression of blood group systems ABO and Rh [60] will need at least a 5 to 10 year period of research.

References

- [1] Remy B, Deby-Dupont G, Lamy M. Red blood cell substitutes: fluorocarbon emulsions and haemoglobin solutions. *Br Med Bull* 1999; 1: 277-98.
- [2] Spahn DR, Kocian R. Artificial O₂ carriers: status in 2005. *Curr Pharm Des* 2005; 11: 4099-114.
- [3] Lowe KC. Blood substitutes: from chemistry to clinic. *J Mater Chem* 2006; 16: 4189-96.

- [4] Clark LC, Gollan R. Survival of mammals breathing organic liquids equilibrated with oxygen at atmospheric pressure. *Science* 1966; 152: 1755-1756.
- [5] Riess JG, Le Blanc M. Perfluoro compounds as blood substitutes. *Angew. Chem. Int. Ed. Engl.* 1978; 17: 621-634.
- [6] Yokoyama K, Yamanouchi K, Watanabe M *et al.* Preparation of perfluorodecalin emulsion; an approach to the red cells substitute. *Fed. Proc.* 1975; 34: 1478-1483.
- [7] Ingram DA, Forman MB, Murray JJ. Activation of complement by fluosol attributable to the pluronic detergent micelle structure. *J. Cardiovasc. Pharmacol.* 1993; 22: 456-461.
- [8] Tremper KK, Friedman AE, Levine EM, Lapin R, Camarillo D. The preoperative treatment of severely anemic patients with a perfluorochemical oxygen-transport fluid, Fluosol-DA. *N Engl J Med.* 1982; 307: 277-283.
- [9] Mitsuno, Ohyanagi H. Present status of clinical studies of Fluosol-DA 20% in Japan. *Int. Anesthesiol. Clin.* 1985; 23: 169-184
- [10] Riess JG, Krafft MP. Elaboration of fluorocarbon emulsions with improved oxygen carrying capabilities. *Adv Ex. Med Biol.* 1992; 371: 465-472.
- [11] Faithfull NS. Oxygen delivery from fluorocarbon emulsions – aspects of convective and diffusive transport. *Biomater Artif Cells Immobil Biotechnol.* 1992; 20: 797-804
- [12] Spahn DR, Waschke KF, Standl T, Motsch J, Van Huynegem L, Welte M, Gombotz H, Coriat P, Verkh L, Faithfull S, Keipert P; European Perflubron Emulsion in Non-Cardiac Surgery Study Group. Use of perflubron emulsion to decrease allogeneic blood transfusion in high-blood-loss non-cardiac surgery: results of a European phase 3 study. *Anesthesiology* 2002; 97: 1338-1349.
- [13] Maevsky E, Ivanitsky G, Bogdanova L, Axenova O, Karmen N, Zhiburt E, Senina R, Pushkin S, Maslennikov I. Clinical results of Perftoran application: present and future. *Artif Cells Blood Substit Immobil Biotechnol.* 2005; 33: 37-46
- [14] Durnovo EA, Furman IV, Pushkin SY, Maslennikov IA, Bondar OG, Ivanitsky GR. Clinical results of the application of perftoran for the treatment of odontogenous abscesses and phlegmons in the maxillofacial region. *J Cranio Maxillofacial Surg.* 2008; 36: 161-172.
- [15] Verdin-Vasquez RC, Zepeda-Perez C, Ferra-Ferrer R, Chavez-Negrete A, Contreras F, Barroso-Aranda J. Use of perftoran emulsion to decrease allogeneic blood transfusion in cardiac surgery: clinical trial. *Artif Cells Blood Substit Immobil Biotechnol.* 2006; 34(4): 433-54.
- [16] Faithfull NS. Mechanisms and efficacy of fluorochemical oxygen transport and delivery. *Artif Cells Blood Substit Immobil Biotechnol.* 1994; 22: 181-197
- [17] Edwards CM, Lowe KC, Rohlke W, Geister U, Reuter P, Meinert H. Effects of a novel perfluorocarbon emulsion on neutrophil chemiluminescence in human whole blood. *Artif Cells Blood Substit Immobil Biotechnol.* 1997; 25: 255-260
- [18] Flaim SI. Pharmacokinetics and side effects of perfluorocarbon-based blood substitutes. *Artif Cells Blood Substit Immobil Biotechnol.* 1994; 22: 1043-1054.
- [19] Von Stark. Die resorbarkeit des haimatins und die bedeutungder hemoglobin-preparate. *Dtsche Med Wochenschr* 1898; 24: 805-808.

- [20] Sellards AW, Minot GR. Injection of hemoglobin in man and its relation to blood destruction with especial reference to the anemias. *J Med Res* 1916; **34**: 469-494.
- [21] Amberson WR. Blood substitutes. *Biological Reviews* 1937; **12**: 48-52.
- [22] Amberson WR, Jennings JJ, Rhode CM. Clinical experience with hemoglobin-saline solutions. *J Appl Physiol* 1949; **1**: 469-489.
- [23] Rabiner SF, O'Brien K, Peskin GW, Friedmand LH. Further studies with stroma-free hemoglobin solution. *Ann Surg* 1970; **171**: 615-622.
- [24] Savitsky JP, Doczi J, Black J, Arnold JD. A clinical safety trial of stroma-free hemoglobin. *Clinical Pharmacology Therapeutics* 1978; **23**: 73-80.
- [25] Deby-Dupont G, Remy B, Lamy M. Oxygen carriers: Hemoglobin-based solutions. In: *Transfusion medicine and alternatives to blood transfusion- NATA (Network for advancement of transfusion alternatives)*, Paris: R&J Editions Médicales, 2000: 298-311.
- [26] Riess JG. Oxygen carriers ("blood substitutes") – raison d'être, chemistry, and some physiology. *Chem Rev* 2001; **101**: 2797-920.
- [27] Chang TMS. Future prospects for artificial blood. *Trends Biotechnol.* 1999; **17**: 61-7.
- [28] Benesch R, Benesch RE. Intracellular organic phosphates as regulators of oxygen release by haemoglobin. *Nature* 1969; **221**: 618-22.
- [29] 16. Looker D, Abbott-Brown D, Cozart P, et al. A human recombinant haemoglobin designed for use as a blood substitute. *Nature* 1992; **356**: 258-60.
- [30] Gottfried DS, Manjula BN, Malavalli A, et al. Probing the diphosphoglycerate binding pocket of HbA and HbPresbyterian (beta 108Asn --> Lys). *Biochemistry* 1999; **38**:11307-15.
- [31] Larbuisson R, Deby-Dupont G, Lamy M. Oxygen carriers in cardiac surgery. *TATM* 2005; **7**: 42-57.
- [32] Shirley PJ. Fluids as oxygen carriers and the potential role in trauma resuscitation. *Trauma* 2008; **10**: 139-47.
- [33] Lamy ML, Daily EK, Brichant JF, et al. Randomized trial of diaspirin cross-linked hemoglobin solution as an alternative to blood transfusion after cardiac surgery. The DCLHb Cardiac Surgery Trial Collaborative Group. *Anesthesiology* 2000; **92**: 646-56.
- [34] Schubert A, Przybelski RJ, Eidt JF, et al. Diaspirin-crosslinked hemoglobin reduces blood transfusion in noncardiac surgery: a multicenter, randomized, controlled, double-blinded trial. *Anesth Analg* 2003; **97**: 323-32.
- [35] Kerner T, Ahlers O, Veit S, et al. DCL-Hb for trauma patients with severe hemorrhagic shock: the European "On-Scene" Multicenter Study. *Intensive Care Med* 2003; **29**: 378-85.
- [36] Sloan EP, Koenigsberg M, Gens D, et al. Diaspirin cross-linked hemoglobin (DCLHb) in the treatment of severe traumatic hemorrhagic shock: a randomized controlled efficacy trial. *JAMA* 1999; **282**: 1857-64.
- [37] Shoemaker S, Gerber M, Evans G, et al. Initial clinical experience with a rationally designed genetically engineered recombinant human hemoglobin. *Artif Cells Blood Substit Immobil Biotechnol* 1994; **22**: 457-65.

- [38] Hayes JK, Stanley TH, Lind GH, et al. A double-blind study to evaluate the safety of recombinant human haemoglobin in surgical patients during general anesthesia. *J Cardiothorac Vasc Anesth* 2001; 15: 593-602.
- [39] Winslow RM. Current status of oxygen carriers ("blood substitutes"): 2006. *Vox Sang* 2006; 91: 102-10.
- [40] Greenburg AG, Kim HW. Hemoglobin-based oxygen carriers. *Critical Care* 2004; 8(Suppl 2): S61-S64.
- [41] Jahr JS, Mackenzie C, Pearce LB, Pitman A, Greenburg AG. HBOC-201 as an alternative to blood transfusion: efficacy and safety evaluation in a multicenter phase III trial in elective orthopedic surgery. *J Trauma* 2008; 64: 1484-97.
- [42] Freilich D, Pearce LB, Pitman A, Greenburg G, Berzins M, Bebris L, Ahlers S, McCarron R. HBOC-201 vasoactivity in a phase III clinical trial in orthopedic surgery subjects—extrapolation of potential risk for acute trauma trials. *J Trauma* 2009; 66(2): 365-76.
- [43] Gould SA, Moore EE, Hoyt DB, et al. The first randomized trial of human polymerized hemoglobin as a blood substitute in acute trauma and emergent surgery. *J Am Coll Surg* 1998; 187:113-20.
- [44] Gould SA, Moore E, Hoyt DB, et al. The life-sustaining capacity of human polymerized hemoglobin when red cells might be unavailable. *J Am Coll Surg* 2002; 195: 445-52.
- [45] Jahr JS, Varma N. PolyHeme. Northfield Laboratories. *Idrugs* 2004; 7:478-82.
- [46] Moore EE, Moore FA, Fabian TC, et al.; PolyHeme Study Group. Human polymerized hemoglobin for the treatment of hemorrhagic shock when blood is unavailable: the USA multicenter trial. *J Am Coll Surg* 2009; 208(1): 1-13.
- [47] Moore EE, Johnson JL, Moore FA, Moore HB. The USA multicenter prehospital hemoglobin-based oxygen carrier resuscitation trial: scientific rationale, study design, and results. *Crit Care Clin* 2009; 25(2): 325-56.
- [48] Winslow RM. Cell-free oxygen carriers: scientific foundations, clinical development, and new directions. *Biochim Biophys Acta* 2008; 1784(10): 1382-6.
- [49] Vandegriff KD, Malavalli A, Wooldridge J, et al. MP4, a new non-vasoactive polyethylene glycol-hemoglobin conjugate. *Transfusion* 2003; 43: 509-16.
- [50] Olofsson C, Nygard EB, Ponzer S, et al. A randomized, single blind, increasing dose safety trial of an oxygen-carrying plasma expander (Hemospan®) administered to orthopedic surgery patients with spinal anesthesia. *Transfus Med* 2008; 18: 28-39.
- [51] Olofsson C, Ahl T, Johansson T, et al. A multicenter clinical study of the safety and activity of maleimide-polyethylene glycol-modified hemoglobin (Hemospan®) in patients undergoing major orthopedic surgery. *Anesthesiology* 2006; 105:1153- 63.
- [52] Natanson C, Kern SJ, Lurie P, Banks SM, Wolfe SM. Cell-free hemoglobin-based blood substitutes and risk of myocardial infarction and death. *JAMA* 2008; 299: 2304-12.
- [53] Reeder BJ, Svistunenko DA, Cooper CE, Wilson MT. The radical and redox chemistry of myoglobin and hemoglobin. *Antioxid Redox Signal* 2004; 6: 954-66.

- [54] Balla J, Jacob HS, Balla G, et al. Endothelial cell heme uptake from heme proteins: induction of sensitization and desensitization to oxidant damage. *Proc Natl Acad Sci U S A* 1993; 90: 9285-9.
- [55] Everse J, Hsia N. The toxicities of native and modified hemoglobins. *Free Radic Biol Med* 1997; 22: 1075-99.
- [56] Chang TMS. Blood substitutes based on nanobiotechnology. *Trends Biotechnol* 2006; 24: 372-7.
- [57] Douay L, Andreu G. Ex vivo production of human red blood cells from hematopoietic stem cells: what is the future in transfusion? *Transfus Med Rev* 2007; 21: 91-100.
- [58] Lu SJ, Feng Q, Park JS, et al. Biological properties and enucleation of red blood cells from human embryonic stem cells. *Blood* 2008; 112: 4475-84.
- [59] Harding FJ, Cameron CM, Hu WS, Kaufman DS. Scaleable production of hematopoietic cells suitable for transfusion from human embryonic stem cells in a stirred bioreactor system. *Blood (ASH Annual Meeting Abstracts)*, Nov 2006; 108: 728.
- [60] Douay L. Cell culture for transfusion purposes: the concept of “cultured red blood cells”. *Transfus Clin Biol* 2009; 16: 134-137.

Tables

Table 1: Advantages and problems with perfluorocarbon emulsions used as blood substitutes

• Easy access and moderate cost, long time storage
• No acute toxicity (if small particles), no antigenicity, moderate viscosity, not metabolized
• High density, limited intravascular persistence
• Need of $FiO_2 = 1$: local hyperoxia?
• Phagocytosis of vesicles, RES overload, tissue persistence
• Interference with laboratory tests (opalescent plasma)
• Flu-like syndrome, platelet aggregation, digestive side-effects

Table 2: Sources of haemoglobin molecules used to prepare free haemoglobin solutions

Source of haemoglobin	Technical way of obtention
Human blood	Hb extraction from outdated donor blood and modification of Hb molecule
Cow blood	Hb extraction from slaughterhouse cow blood
Micro-organisms (genetic engineering)	Genetic modification of bacteria, fungi or plants to produce Hb
Transgenic animals	Introduction of human Hb genes in animal foetus and production by mature individuals

Table 3: Free haemoglobin (Hb) solutions (trade name, company and main characteristic) which reached clinical trials

HBOC: haemoglobin-based oxygen carrier; PHP: pyridoxalated Hb polyoxyethylene;
PEG: polyethylene glycol

Name	Company	Characteristics	Clinical trials
HemAssist	Baxter Healthcare	Cross-linked (a-a)Hb	Discontinued; safety (increased mortality)
Optro	Somatogen- Baxter	Human recombinant Hb	Discontinued; safety (hypertension)
Polyheme	Northfield Laboratories	Polymerized human Hb (glutaraldehyde, pyridoxal)	Phase III (trauma, surgery)
Hemopure (HBOC-2001)	Biopure Corp.	Polymerized bovine Hb (glutaraldehyde)	Phase III (orthopedic surgery); ® in South Africa
Hemolink	Hemosol Inc.	Polymerized cross-linked human Hb (o-raffinose)	Discontinued; safety (myocardial infarction)
PHP	Ajinomoto/Apex Bio	Conjugated hum Hb (PEG, pyridoxal)	Phase III septic shock
PEG-Hb	Enzon	PEG-Conjugated bovine Hb	Discontinued
Hemospan	Sangard	PEG-Conjugated human Hb	Phase III elective surgery

Table 4: Side-effects encountered with the administration of free haemoglobin (Hb) solutions and their possible causes

MethHb: methaemoglobin; NO: nitric oxide; ROS: reactive oxygen species; gastrointestinal tract

Side-effect of HBOC	Possible cause
Vasoconstriction (increase in systemic and pulmonary arterial pressure and vascular resistance)	NO scavenging, activation of endothelin production, direct stimulation of alpha adrenergic receptors
Cardiovascular events (myocardial infarction)	NO scavenging? Direct toxicity on organ?
Nephrotoxicity (oliguria, haematuria)	Direct toxicity leading to kidney dysfunction (tubular necrosis and obstruction)
Neurotoxicity	Direct toxicity on organ?
Increase in blood levels MethHb (ROS)	Hb autoxidation (during storage or in vivo?)
"Jaundice-like" syndrome	Hb extravasation (endothelial cells, tissues)
Bilirubinemia	Hb destruction (short intravascular lifetime, overload of plasma elimination capacity)
GI (abdominal discomfort, pain, nausea, vomiting)	Binding of NO? Direct intestinal toxicity?
Elevation of liver & pancreatic enzymes	Direct organ toxicity? NO binding?
Increased bacterial virulence	Iron supply
Interference with macrophage functions	Blocking by binding of Hb-haptoglobin complexes to receptors?
Activation of complement, kinin and coagulation cascades	NO scavenging leading to platelet aggregation?
Immunogenicity	Xenogeneic Hb, polymerized Hb
Interference with laboratory tests	"Haemolysis-like" effect