(2006) EMBO Reports 7, 562-566

Life, chemistry, and cognition

Conceiving life as knowledge embodied in sentient chemical systems may provide novel insights into the nature of cognition

Ladislav Kováč
Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia. E-mail: kovacl@fns.uniba.sk

The very first existential and ontological evidence of a human individual is suffering. As Shakespeare put it in one of his plays, no philosopher would patiently endure a toothache. Under unbearable externally provoked pain or distress even the staunchest advocate of solipsism may refrain from the claim that the world is an illusion. What makes suffering so convinsing is the fact that we experience it; we do not merely observe it. "I experience, hence I am" would be a more appropriate description of the indisputable human condition than the classical "I think, hence I am".

The latter statement was a foundation stone of the conception of the world by René Descartes (Cartesius) (1596-1650). Thinking for him was the exclusive capacity of the incorporeal mind, the soul, which he defined as a thinking substance. Only humans had the soul, only they could reason; all other organisms, including the monkeys (as he explicitly posited), were mere automatons. Descartes did not deny life to animals; he did not equate them with human-made machines, as has been often imputed to him. In contrast to inanimate machines, animals had the corporeal spirits, which humans had too, and exhibited sensations and "passions". He proposed an intriguing mechanism of how the spirits commanded the body. But, in his view, all behaviour of non-human animals could easily be explained from the constitution of their organs solely; they did not possess any capacity of pure thought, which was freed of natural impulses and passions, they missed understanding. He referred with approval to the ancient Greek philosopher Epiktetos that you are not your body; a body is just finely moulded clay.

René Descartes preceded Isaac Newton by 50 years and Charles Darwin by 230 years. For his time, his mechanistic explanation of how the body works and how the mind communicates with the brain was ingenious. Chemistry as a science did not exist. The clock was the best model of the body. At the same time, in the absence of effective medicine, long before analgesia and anaesthesia were invented, neglect, contempt, rejection of the body, the identification of the "I" with a pure reflective soul, may have been a cunning way for the noblest and wisest among humans of how to belittle humiliation imparted by permanent bodily troubles and preserve one's own serenity and dignity. This attitude can be traced as back as to Plato, and so classical rationalism, a major current of the European thought, the procreator of science, may have had here one of its sources. A sophisticated, modern incarnation of Descartes' dualism may be the "computational model" of cognition: mind is like a software program and the brain like hardware. This model has dominated cognitive science – or, as George Miller (2003) prefers to call it, cognitive sciences, in the plural – for the last few decades. In fact, the advancement of science has nowadays brought cognitive sciences to the fore of scientific inquiry. A large part of the community of cognitive scientists keep considering cognition as the exclusive property of humans, the human mind being the organ of conscious perception, thinking, and memory, busy with "information processing". The basic constituents of consciousness are ideas, judgments, propositions. The mind is no longer "incorporeal", the brain is its "structural and functional realisation" (Miller, 2003), but, in principle, there is no reason why its representational and computational capacities cannot be embodied in other kind of "hardware", including the human-made computers. This is why the field of computer science and of artificial intelligence became an important part of cognitive sciences. The clock has been replaced by the computer as the model of the brain, and even of life as a whole.

Yet, at least three conceptual shifts may nowadays represent radical departures from the Cartesian tradition. First, "affective revolution" appears to be underway. Emotions are no longer considered as unimportant, or as impeding, contaminations of cognition, but as the inseparable, or even central part of it. Consciousness itself may be the matter of emotion more than of reasoning. No longer the brain in a form of a computing machine, but the entire body is seen as the organ of cognition. No wonder that one of the leading protagonists of the affective revolution, Antonio Damasio, has given his book the title "Descartes' error" (Damasio, 1995). Second, the role of unconsciousness, once accentuated by Sigmund Freud, is being reinterpreted: even in humans, conscious deliberation may represent just a "monomolecular layer" on the immense "ocean" of what T. D. Wilson (2002) named "the adaptive unconscious". Third, cognition is being analyzed in an evolutionary perspective, under the name of "evolutionary epistemology". Cognition is no longer an exclusive capacity of humans, but life is equated with cognition, and biological evolution as a whole is the evolution of cognition (Radnitzky & Bartley, 1987).

In the "horizontal" approach to cognition, represented by evolutionary epistemology, cognition was supposed to have begun with the very origins of life. Famous has become the statement of one of its founder, Karl Popper: "From the amoeba to Einstein, the growth of knowledge is always the same..." How about adopting a "vertical" approach, orthogonal to that of evolutionary epistemology? To start from a conscious human individual and ascend in analysis up to community, society, and eventually the entire universe? And also to proceed in an opposite direction, descending through the layers of ever lower complexity, tissues, cells, down to the molecules? At which level the concept of cognition, with its inventory of consciousness, cogitation, feeling, perceiving, sensing – and even living – would lose meaning and would only correspond to nomic lifeless interactions? The vertical approach to cognition has been named "cognitive biology" (Kováč, 2000) and may be a complement to evolutionary epistemology (Fig. 1). One of its fundamental principles has been called the "principle of minimum complexity" or "Delbrück's principle". It recalls the feat of Max Delbrück, who laid foundation of modern genetics by not studying complex human heredity but rather heredity proper to simple phage molecules. Incidentally, Delbrück had also started to study cognition and behaviour by using simple fungi *(Phycomyces)* as model organisms. Brian Goodwin (1978), who may have invented the term "cognitive biology", considered cognition arising from the purposeful interplay of a system of molecules. But it was Jacques Monod (1970) who may have been the first to propose that cognition can be present already at the level of single molecules, specifically protein molecules: their capability of discrimination may be visualized as a sort of cognition.

The fashion of presumed modelling of cognition, and also life as a whole, on a computer has often seduced cognitive scientists to an illusion that they need not worry about logistical issues such as energy and physical construction, dispense with the austere universe of thermodynamic constraints, and focus of what they may have considered as fundamental questions of information flow. Only lately the idea that cognition is embodied, and that the fact of embodiment cannot be bracketed, is gaining weight. For cognitive biology, cognition not only is embodied, but its embodiment has a specific form: life as we know it, natural life (n-life), is a chemical system and cognition is a property of such a chemical system. Logical possibility does not equal thermodynamic feasibility. Even virtual life (v-life), which thrives at the computer screens of those who model n-life, is embodied; although it is not chemical but electromagnetic. Neither artificial life (a-life), which soon may be invented by humans and once perhaps displace the n-life on Earth, need be founded on chemical principles, it may well function in the form of electromagnetic, and even purely mechanical, systems. In an authoritative review of the history of cognitive sciences, Miller (2003) presented an instructive picture of six disciplines which presumably took part in the constitution of cognitive science. Chemistry was absent in the scheme. In fact, however, it would be appropriate to place chemistry in the centre of all of them, if we want to describe n-life, and cognition as one of its attributes (Fig. 2). To paraphrase Galileo, who said that nature is written in the language of mathematics, biologists should keep in mind that natural life is written in the language of chemistry.

As stated in a standard textbook (Bazarov, 1983, p. 235), "chemical processes are the simplest of various natural processes, ... fluxes are directed to the state of equilibrium and do not flow in space coordinates but in coordinates of the composition of the system." Thus, standard chemical processes are scalar. Centuries ago, alchemists used to say that compounds do not react unless dissolved (*Corpora non agunt nisi soluta*), but even one of the founding fathers of modern biochemistry, Otto Warburg, was convinced that "where structure begins, biochemistry ends" (quoted by Kornberg, 1989, p. 66).

This, however, is not the case. In contrast to standard chemical reactions, biochemical processes are not scalar, but intrinsically vectorial. As discovered by Mitchell (1961), "vectorial metabolism is represented by a network of spatio-temporal pathways along which ligands (including solutes, ions, chemical groups, electrons, catalytic compounds and complexes) are conducted by articulated movements that occur in the direction of the thermodynamically natural escaping tendency, corresponding to the vectorial (or higher tensorial order) resultants of the thermodynamic and field-effect forces acting on the ligands." It still may evade to many biologists that Peter Mitchell has accomplished in biology, a century after the advent of the idea of evolution by natural selection, a breakthrough no less important than had been the breakthrough of Charles Darwin.

The magic of biochemical vectoriality resides in the nature and structure of proteins. A native protein molecule is a spatially asymmetric construction, in which many weak electrostatic, hydrogen, hydrophobic and van der Walls attractions sum up into a strong attractive force. Because of this multiple summing, a typical protein should be an extremely rigid substance, perhaps more rigid than steel. However, the strong chemical force is balanced by an equally strong dispersive force of entropy. This energy-entropy compensation makes of a protein a uniquely labile, and, at the same time, remarkably robust, structure. As explained by Frauenfelder et al. (2003), "a protein does not exist in a unique conformation, but can assume a very large number of conformational sub-states". As they put aptly, "if a protein had just a single conformation, it could not function and would be dead like a stone." The conformation sub-states are not random. Each of the proteins we encounter in nature is a product of evolution; it has been selected to perform a goal-directed, teleonomic function (Monod, 1970). It holds probably for the the majority of natural proteins that the function of a protein molecule begins with a specific binding of a low- or high-molecular ligand. But it is not the protein molecule that is selecting the appropriate ligand. Slow structural motions between sub-states are running all the time, also in the absence of ligand, and, when the ligand is present, it binds to one sub-state chosen from all those displayed by the protein molecule. There is no exaggeration to say that a protein molecule exhibits exploratory behaviour. The intrinsic, goal-directed plasticity of the protein molecule can be dubbed "molecular sentience”. It is this sentience that makes protein a “living” molecule. Traditionally, this privilege has been attributed to DNA, but, according to Lewontin (1992), DNA is a dead molecule, one of the least reactive. This reminds of a statement of Robert Rosen (1991) who anchored biology entirely in what August Weismann called the soma: the soma is what is alive. We have to admit that the essence of life is sentience, a capacity to exhibit a variety of potential internal states, selected in evolution, and contingent upon the state of the immediate environment.

It is the teleonomy built in the protein structure by evolution that gives reason to name protein-ligand interaction “molecular recognition”. Only those molecular interactions deserve this name that are teleonomic. Because of this intrinsic teleonomy, a protein gives meaning, significance to its environment, that is, to its ligand. Nomic interactions of atoms and molecules, such as chemical reactions in the inanimate world, with no evolutionary history, are inevitable, deterministic, timeless, and do not represent recognition. But molecular recognition by a protein molecule is only part of the story. Recognition is followed by an action. A ligand is a signal. In contrast to standard chemical interactions, binding energy is not fully dissipated as heat, but a portion of it is utilized for doing molecular work – a specific, pre-programmed, change in the conformation of the protein molecule. In this way, the signal is transmitted from one site of the protein molecule to another site. The transmission takes place in the four-dimensional space (which involves also time as a coordinate) and it is this process that gives biochemistry its vectoriality. The exploitation of binding energy was originally applied to enzyme catalysis, where a portion of binding energy serves to lower activation energy of a reaction (Jencks, 1975), but its enlargement to account for the work of translocators, receptors, transcription factors is straightforward.

By receiving and transmitting signal, protein executes a complete working cycle, and it does it in the “all-or-none” fashion. It is appropriate to consider most protein molecules as molecular engines. The cycle constitutes molecular cognition. Hence, molecular cognition consists in molecular sensation (which has two inseparable aspects, recognition and signifaction) and molecular action. As Monod (1970) pointed out, some proteins, by specific binding two or more ligands, can bring ligands together not on thermodynamic, but exclusively on logical (teleonomic) grounds (the principle of gratuity). By selective binding, proteins associate with each other to form teleonomic protein networks. In addition, because of their structural asymmetry, protein molecules can channel thermal energy of their surroundings to do work as Brownian ratchets. It is essential to acknowledge that all the activities of a protein reside already in its structure, built-in by evolution. In terms of Shannon’s communication theory, exploratory behaviour of a protein molecule, motion between sub-states, is a manifestation of its information entropy. The appropriate ligand triggers pre-programmed response(s); the whole process is no more but a one-bit information transaction.

The principles of cognition at the basic, molecular, level seem to apply to cognition at all other levels. Cellular cognition consists of the operation of a set of molecular sensors as modules, and the network of cellular cognitive devices constitutes cognition at the level of the individual organism. Indeed, there are a number of levels of nesting lower-level entities within higher-level individuals (Gould, 2002). In the vertical optics, life appears as a Russian doll; it comprises a number of more or less loosely bound modules and it exhibits multi-layer nestedness (Fig. 3). At higher levels, sentience means sensitiveness and excitability, but largely continues to consist in exploration by displaying pre-programmed (as a result of either evolution or of development) alternatives. Living entities are semantically closed (Rosen, 1991); only humans, thanks to artefaction and the evolution of culture may be an exception, but much less than one may assume. This reminds us of Plato, for whom all knowledge was just “recollection” of the soul, and of Johan W. Goethe, who remarked that “we see only what we know”. In bacterial chemotaxis, movements in all directions are modulated by ligand binding, resulting in a biased random walk. Working of the immune system is an example of sentience at a higher level. Stochastic gene expression (which is not random in the common statistical sense; it is circumscribed by construction constraints) may be another example, just as is synaptogenesis, in which many possible neural connections are being displayed but only part of them, those “approved” by the input from the environment, are retained. Incidentally, at these higher levels, the same principle applies as has been mentioned in the case of a single molecule of protein sensors: the signal merely triggers a response but does not contain information about what response should be (Kirschner & Gerhart, 2005). Therefore, the use of terms borrowed from the theory of communication, including “channel capacity” or “information processing”, and also analogies from linguistics, may be misleading at all levels, with the exception of the genuine human communication systems.

According to Feinberg (2001), “the brain is arranged in the same nested hierarchy as all biological systems. From this structure emerges the unified self.” As inferred from a study on vision in mammals, specific neurons may exhibit spontaneous patterns of activity that resemble representations of visual stimuli; such intrinsic cortical states may embody the brain’s “hypotheses” about the state of the external world, which are continuously updated by the received visual data (Kenet et al., 2003). Operant conditioning is based on displaying various pre-programmed behaviours and stabilization of one of them. Scaruffi (2000) hypothesized that all possible states of emotions may be produced randomly all the time and the environment “selects” which ones have to survive. At all levels, cognition continues to be a dual process of sensation and action. At the highest levels, the action need not be overt. In human cognition, acting may become fully internalized in the form of thoughts: thinking, like dreaming, may be conceived as abstract motor activities; according to Konrad Lorenz (1943), as “das Hantieren im Vorstellungsraum” (handling in the imagination space).

There is much less “information processing” than it is assumed by the “life-as-information” or “life-as-computation” metaphor that has dominated biology for the last 50 years. Constructions at all levels, from protein molecules, through cells, tissues, individual organisms, up to social institutions and culture represent embodied knowledge that has been accumulating and retained in evolution by natural selection. Triggering of pre-determined responses, and, indeed, selection from them, seems to be a more appropriate description than information processing. Chemistry, more than any other science, abounds in emergences; as a matter of fact, chemistry is a science of qualities and may be called a “science of emergence”. When molecules of hydrogen and oxygen react to produce molecules of water, a substance with novel, different properties emerges from the reaction. Just because life is a chemical system, emergent phenomena at various levels of hierarchy are as natural, but also as unpredictable, as inevitable, and as unequivocal, as is the emergence of water from hydrogen and oxygen. The brain itself is a chemical system: not a computer with hardware and software, but rather a “wetware” (Kosslyn and Koenig, 1995). Perceptional and emotional qualia, and even consciousness, including self-consciousness, lose much of their mystery if we conceive them as emergencies in complex chemical systems, in which myriads of teleonomic chemical interactions – molecular cognitions – are running all the time.

Cognitive biology, as much of reflexion on life, mind, and consciousness, is more a reinterpretation of the existing data than a research program offering new experimental approaches to the age-old problems. One can ask with Tom Wolfe (2000): “Why wrestle with Kant’s God, freedom, and immortality when it is only a matter of time before neuroscience, probably through brain imaging, reveals the actual physical mechanism that fabricates these mental constructs, these illusions?” The answer is at least threefold. First, our psychological constitution does not allow us to wait patiently until science will have provided us with all the answers to our vital questions; to achieve peace of mind, humankind has always strived for unified, all-embracing understanding. In our time, the rapid progress of science enables us to quickly up-grade our interpretations, however transitory, to fit the state of knowledge achieved. Second, the insight provided by cognitive biology may help us cope with a constraint imposed upon our understanding of the human brain that has been named "Kuhlenbeck's paradox" (Gerlach, 1988): our world of consciousness is a phenomenon of the brain, but our brain is also a phenomenon of the brain; hence, a closure reminiscent of Kurt Gödel's incompletness theorem for first order arithmetic with its corollary that the consistency could only be proved in a richer metasystem. We would need some divine "metabrain" to achieve a full comprehension of the human brain. Yet, the analysis of cognition of less complex organisms or the analysis at less complex levels may permit us to extrapolate this knowledge towards human cognition and in this way circumvent the Kuhlenbeck's barrier.

The third answer brings us back to where this essay started. The existential primordial of human suffering may have been the driving force behind science: from a specific angle, science seen backwards appears to be a history of efforts to reduce human suffering. Why not make this mission explicit and central to science? Then, of course, a proper understanding of human cognition, with its major and inseparable constituent, emotions, is a prerequisite to achieve the goal. The import of such understanding may be far-reaching. As the poet André Breton expressed, a mistake in the explication of man causes an error in the explication of the universe. It has been pointed out that the longed-for "theory of everything" may turn out not to be the final theory of the fundamental elements of the world but the theory of mind and of its relation to the universe.

References

Bazarov IP (1983) *Termodinamika*. Moscow: Vysshaya shkola

Damasio A (1995) *Descartes' error. Emotion, reason, and the human brain*. New York: Putnam's sons

Feinberg T (2001) *Altered egos*. Oxford: Oxford University Press

Frauenfelder H, McMahon BH, Fenimore PW (2003) Myoglobin: The hydrogen atom of biology and a paradigm of complexity. *Proc Natl Acad Sci US* **100:** 8615-8617

Gerlach J (1988) Gödel-Theorem and Kuhlenbeck-Paradox. *Naturwissenschaften* **75:** 393-398

Gould SJ (2002) *The structure of evolutionary theory.* Cambridge, MA: Harvard University Press

Goodwin BC (1978) A cognitive view of biological process. *J Soc Biol Structures* **1:** 117-125

Jencks WP (1975) Binding energy, specificity, and enzyme catalysis: The Circe effect. *Adv Enzymol* **43:** 219-410

Kenet T, Bibitchkov D, Tsodyks M, Grinvald A, Arieli A (2003) Spontaneously emerging cortical representations of visual attributes. *Nature* **425:** 954-956

Kirschner MW, Gerhart JC (2005) *The plausibility of life.* New Haven, CT: Yale University Press

Kornberg A (1989) *For the love of enzymes.* Cambridge, MA: Harvard University Press

Kosslyn SM, Koenig O (1995) *Wet mind: The new cognitive neuroscience*. New York: The free press

Kováč L (2000) Fundamental principles of cognitive biology. *Evolution and Cognition* **6:** 51-69

Lewontin R (1992) The dream of the human genome. *N Y Rev Books*, 28 March, pp. 31-40

Lorenz K (1943) Die angeborenen Formen möglicher Erfahrung. *Z Tierpsychologie* **5:** 235-409

Miller GA (2003) The cognitive revolution: a historical perspective. *Trends in Cognitive Sciences* **7:** 141-144
Mitchell P (1961) Coupling of phosporylation to electron and hydrogen transfer by a chemiosmotic type of mechanism. *Nature* **191:** 144-148
Monod J (1970) *Le hasard et la nécessité*. Paris: Éditions du Seuil
Radnitzky G, Bartley WW (1987) *Evolutionary epistemology, rationality, and the sociology of knowledge*. La Salle: Open Court
Rosen R (1991) *Life itself*. New York: Columbia University Press
Scaruffi P (2000) http://www.thymos.com/science/emotion.html
Wilson T D (2002) *Strangers to ourselves: Discovering the adaptive unconscious*. Cambridge, MA: Harvard University Press
Wolfe T (2000) *Hooking up*. New York: Picador

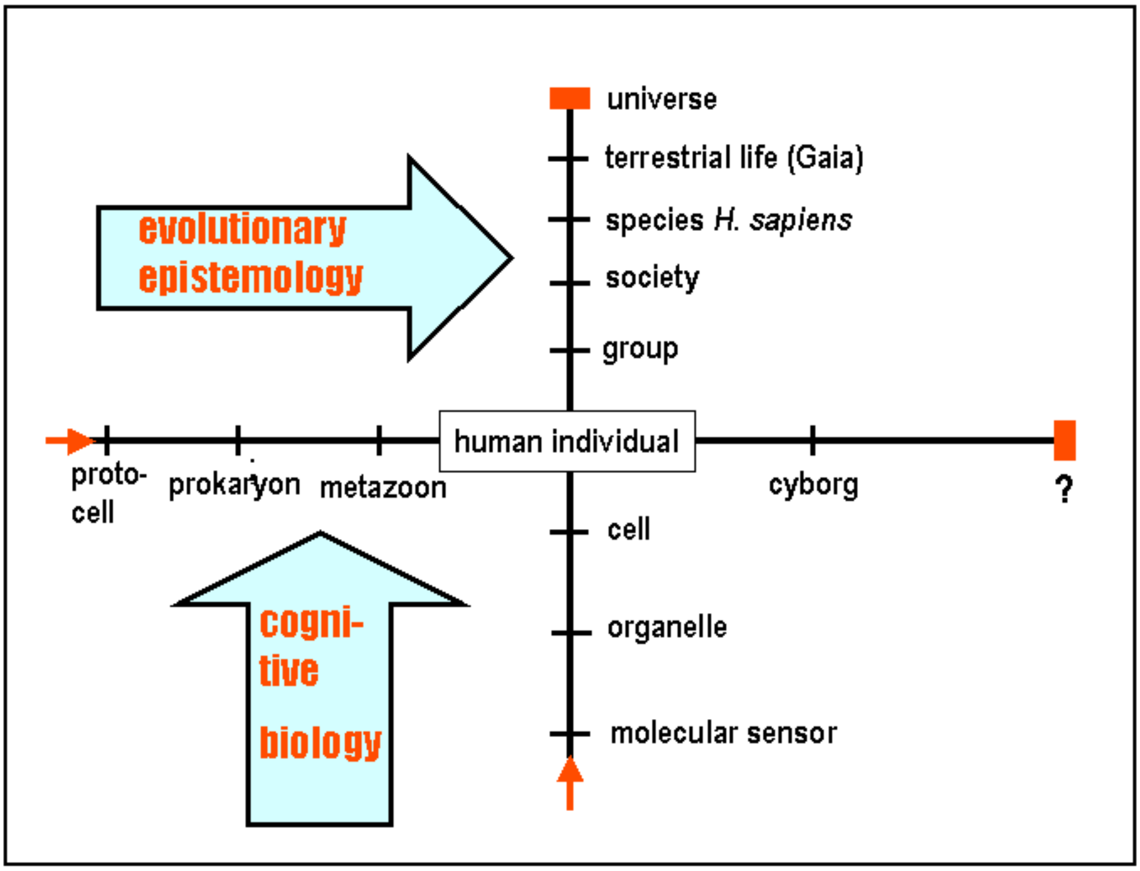

Fig. 1. Cognitive biology is an approach to cognition orthogonal to evolutionary epistemology

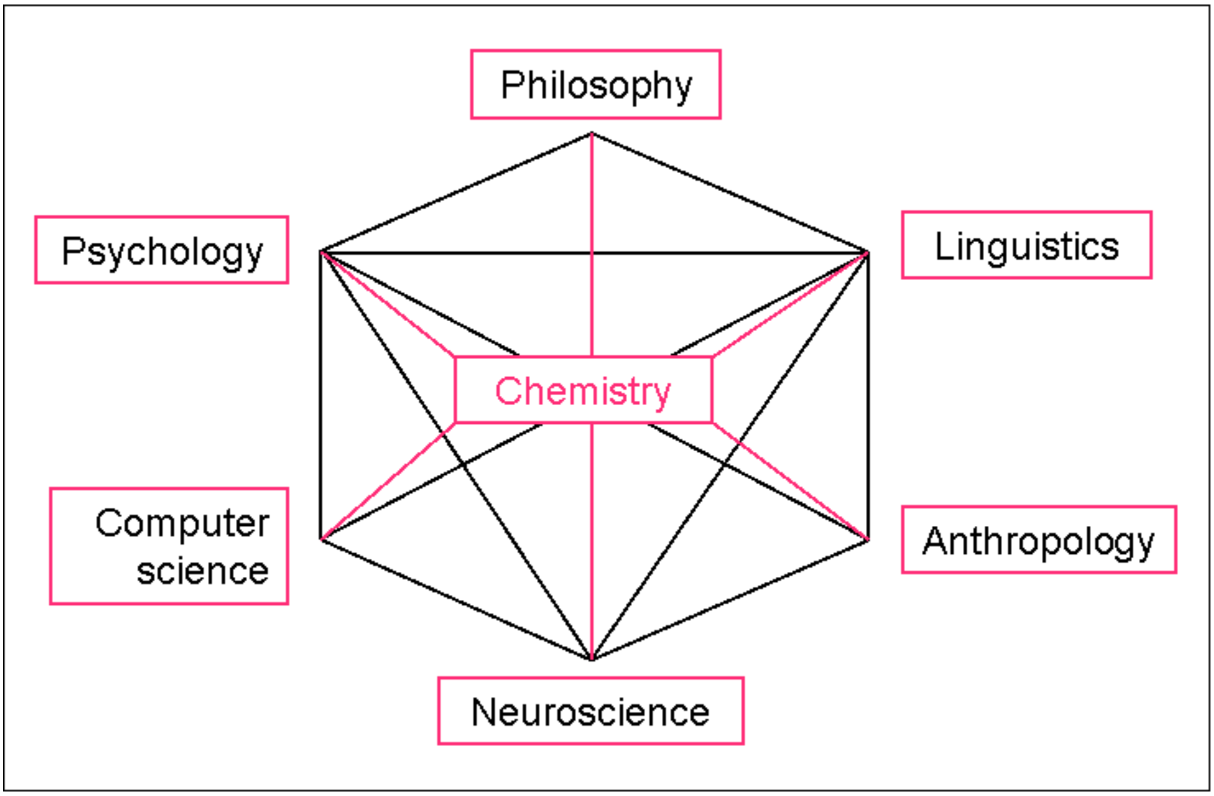

Fig. 2. Scientific disciplines participating in the constitution of cognitive sciences. Modified from Miller, 2003. The original scheme of Miller is in black, modifications are in red.

Fig. 3. Nested levels of biological individuality. Life may be compared to a Russian doll.