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Visions & Reflections

Disrespectful thoughts on dimensions in the outer and inner world

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Without access to English litterature during WW II, I and most others in the occupied countries, believed that the constituents of our body remained there once they were incorporated. Therefore, it was enlightening to read the "The dynamic state of body constituents" a couple of years after the armistice: the advent of the isotope technique had buried this misconception. As looked at on the molecular/atomic level, we are in constant "renewal" – even in the next second are we no longer the same. The atoms/molecules come and go, although not in all eternity. Our genetic programme requires that they shall return to where they derive – "from dust you came, to dust you will go, from dust you shall resurrect".

In the years since, an immense store of data on our body's function, on diseases which attack its wellbeing, and how we can cope with many of them, have accumulated. More so in this period than in all previous times altogether. The progress has been overwhelming and unprecedented. However, this is not the end, it is not even the beginning of the end, but it is, perhaps, the end of the beginning, to quote Churchill. The brain is, despite the millions of published papers, still the big enigma. E.g. we have little idea of the mechanism of the language, inborn to all individuals and that can be understood by everybody all over the globe: the cry and the smile with its fellow laughter. How does crying/weeping convert a painful experience, somatic or psychic, into a tolerable state, and bury it somewhere in the subconscious? Why cannot thinking be stopped at will? Thence, it is impossible not to sin, as the Bible requires not to "sin in thoughts, words and deeds". Although such thoughts may be rapidly repaired by good ones, nobody knows whether a sin is already registered. Similar inexplicable questions may be posed in thousands.

In the forties, our minimum units were one hundred of a ml, mm, mg, mV – only the new tool for structural studies, the electron microscope, allowed us to see a 10^{-6} mm dimension. In physiological chemistry (the term used at that time), colour filters were used to obtain a selection of wavelengths – the Beckman spectrophotometer first came to our laboratory in 1950; plasma proteins were assayed by adding drops to a series of $CuSO_4$ solutions with known specific gravity, the one where the drop came to stand-still indicated the concentration from a worked out standard, and so on. We could not dig deep into the mysteries with methodologies like that. However, we were equally happy as today every time we could add a piece of new knowledge, however small. And we lived in harmony with *concrete* things and phenomena, units were real, comprehensible.

It is not like this any longer. The more we attempt to understand, the more we enter the *abstract* world. The relativity theory (macrocosm) operates with distances in speed of light – light-years, space-time – time with curved shape, gravity having the speed of light, and so on. All concepts appear as pure nonsense! In the microcosm, where quantum mechanics is the guide, we find the same desperate situation: one second is an eternity of time compared to 10^{-43} s (Planck time), length is down to 10^{-34} mm (Planck length)! What a counterpart to billions of years and light-years! How come that the subatomic particles, like quarks, bosons, neutrinos, gravitons etc., can be carriers of the four forces, gravity, electromagnetic, weak and strong nuclear forces, that once released becomes an atomic bomb? All features entirely incomprehensible with our present brain. A consolation is that even the greatest living theoretical physicist, Stephen Hawking, admits that he does not understand it either. Only

through mathematics – the most glamorous of sciences – can those who have the ability, make an imaginary sense out of the calculations. And when experiments and measurements agree with the theory, the truth is secured. Thus, application of the physical and mathematical sciences have lead to understanding the nature of matter, and to explaining the universe in great detail – though not yet entirely. Both achievements to enormous benefit, but also endangering life on earth.

Sadly indeed, our ability to understand is deplorable: what we recognise directly with our senses is very close to negligible, applying to distance, force, sound, speed, time, voltage and vision. The world would look utterly different were we born with X-ray or electron microscopic vision, hearing in the 50 MHz or 0.1 Hz-area, or countless combinations of these and other senses. Wouldn't this also be a reality besides the one we live in? Or, must we adhere to the anthropic view: the universe must be as *we see* it – were it different there would be no one to observe it (Hawking). A rather defeatistic conclusion, though probably true.

But do we need to go outside our own body to find dimensions we cannot easily cope with?

From my own area, blood platelets may serve as example. Their task is to survey and repair the wear, tear and injuries of blood vessels. They derive from an estimated 10^6 megakaryocytes in the bone marrow, and there are 2×10^{11} platelets in the blood with a life time which spans about 8 days. Thus it may be computed that, in thrombocytopenia where production may increase five times, 10 platelets are formed per second per megakaryocyte. This is not an impressive number compared to the physical world. However, the formation of a platelet is not a simple task. After thrombopoetin activates the nucleus, and DNA is induced to code for the multiplicity of proteins to be formed, the following procedures and components are involved: The DNA's are copied to mRNA's/tRNA's/rRNA's which leave the nucleus to induce protein synthesis in the rough endoplasmic reticulum with its ribosomes, passage of these through the smooth endoplasmic reticulum and the Golgi apparatus for strict control of every single molecule with elimination if incorrect, production of the multiplicity of carbohydrates and lipids, many coupled to proteins – needing a long series of enzymes – sorting and packing for further transport, construct the complicated mitochondria with the machinery for energy production, design and build the three granule types with their membranes and fill in a rich variety of electrolytes, signal molecules, growth factors, enzymes and cofactors, synthesise cytoskeletal components like collagen, microtubules, microfilaments, actin, myosin, arrange a complicated transport system, provide glycogen stores, design and produce the cell wall with its protein bilayer and myriades of phospholipids of different types, manufacture of enzymes to govern their important role in platelet function, insert the numerous receptor molecules, many highly complicated, weaving out and in the membrane up to eleven times, construct and insert a multiplicity of ion-, voltage and other channel forming molecules, and so on.

An average-sized protein (60 kDa) contains around 600 amino acid residues (some considerably more than 3000). These must be carefully chosen one by one from a selection of 20 different species to constitute the programmed molecules. Their production further requires a multiplicity of various molecules, polymerase and other specific enzymes for coupling of amino acids, which also need to be manufactured. Additionally, metal ions and cofactors are needed. All these molecules consist of atoms, from 24 in glucose to many thousands in large proteins, that must be of correct nature and installed in the right place and position to enable final formation of tertiary/quarternary states, decisive for its function. Most components appear in multiple copies.

It is miraculous that all these components, estimated to around 500 000 000 molecules, and the millions of complicated processes to finalise a platelet, occur within 0.000 008 l, the volume of a platelet. More impressive is that it takes a small second, indicating that the reaction velocities must be very high, even though many processes are going on in parallel. To estimate a valid mean is not feasible, as we do not know the ratio physical to biochemical reactions. What we know, however, is that a pivotal platelet reaction, adhesion, consists of two conformational changes: first, vessel wall denuded collagen receptor to blood von Willebrand factor, and second, activated vWF to platelet GP II_bIII_a receptor. As conformational changes have now been shown to proceed in $10^{-12 \text{ to } -15}$ s, the start of haemostasis is therefore instantaneous to our mind. And it "detonates" a whole series of changes in the platelet exterior and interior that constitute the repair processes, mainly biochemical and thus slower.

Suffice with another example about biological velocities: Of the about 10^{19} haemoglobin molecules in our body, with erythrocyte life time being 120 days, more than 10^{16} are replaced/day, i.e. close to 10^9 molecules/second!

Although not matching the physical world, these dimensions belong to the same class: incomprehensible, but true.

Neuroscientists maintain that all experiences we have noticed, including the thoughts we have created, if rehearsed initially, are stored more or less for ever. What an unimaginable collection of data it must be! And from e.g. a flight we can, in incredibly short time, revive the landscapes, towns, lakes, food, persons, and other experiences in great detail, each craving time to be reproduced from many parts of the brain and meaningfully coupled together. Seemingly, only extreme velocities may account for the processes behind.

Velocities of a nerve impulse – a main object of study in neuroscience, are not impressing: maximum being 10^2 m/s. However, parallel coupling, minimal distances between the cells, and short regeneration of conductivity all promote the spread of impulses. The bulk of knowledge accumulated on the function of the nervous system is won by studies on this phenomenon. Besides, information has appeared from other biophysical methods, e.g. PET-scans, and approaches like studies of human brain lesions and animal experimentation, including knock out animals. Together with elucidation of biochemical mechanisms, a reasonable, but not yet final theory for this decisive intellectual function exists. Thus, it is established that short- and long term potentiation, synaptic plasticity, dispersion of information to various locations, are important features of the memory process. Furthermore, established *de novo* synthesis of special molecules tells that the genetic system is involved, directly or indirectly. With its 10^{66} possible combinations of the 20 amino acids – each memory could have its own molecule, or its own of the many possible isoforms!

Although storage is a compulsory phenomenon for intellectual activity, the most intriguing problems: the molecular basis for retrieval of this knowledge, for consciousness, and for understanding of other psychological and intellectual activities – are unanswered. When you pose questions about these mechanisms, tautology enters the vocabulary – there is not much substance to offer. The appearance of these capabilities in mankind represented a leap – we departed from animals, creativity was a new ability. As I alluded to above, the velocities of less sophisticated processes seem extreme. And it is reason to assume that velocities in the intellectual processes are no slower – the inverse could as well be expected. Brain cells differ widely from other cells, as do their tasks. Unlike other cells, they are not programmed to reproduce, and as the most complex of all cells they nevertheless form at a speed of 5000 cells per second during foetal life, ending up with 10^{12} at birth. Largely, this number is for life, but they develop both in weight and wisdom, the former three times, the latter very variably, if at all. Why couldn't some other extraordinary characteristics, related to their particular tasks, exist besides "immortality"?

Are the chemical-electrical communication systems enough to account for creativity and other intellectual processes, as many neuroscientists seem to believe? Those mechanisms are as difficult to apprehend as force-bearing invisible particles and curved time. To elucidate these have hitherto necessitated geniuses as Einstein and others. Therefore, I am pessimistic about the possibility of our brain to unravel its own secrets, to me it is a contradictio in adjectio – a new algorithm seems to be needed. A Grand United Theory for the physical world is expected shortly, but not yet ready – will it be? Establishment of the molecular basis for e.g. *what initiates the revival of memories, or, what induces a thought when the eyes are closed, the ears tightened and with no other input from senses*, *or, which " particlewaves" are at play in creative activity* will crave new superbrains, a leap above the former and present, either arising by natural or site directed mutations. Sherrington expresses laconically that "it may take time until an experimental preparation answers your question". The biological basis for love may be somewhat easier to resolve, as it is connected with a more primitive ability, reproduction, where feromons play a pivotal role. However, it may not be wise to strive for this, as the great drama-writer, Henrik Ibsen, held that "when love seeks to comprehend its own selfe, it is lost". And Gerhardus van der Leeuw felt that "the mystery of life is not a problem to be solved, but a reality to be experienced". Nevertheless, the search will certainly go on.

Turning back to the introduction and the dimensions we applied 50 years ago, at maximum 10^{-5} and to present, $10^{-12 \text{ to } 15}$, we have bettered at least 10 000 000 times! If we improve similarly in the next 50 years, which is realistic since accumulation of knowledge by now is exponential, at least some of the riddles may have waned. I would really appreciate to staying alive for so long! (but then I would certainly wish to continue).

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