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On yeasts and men: Piotr P. Slonimski and the science before and after the turn of the millennium

Ladislav Kováč

Center for Cognitive Biology, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia

(…)
Okagnienie trwać będzie tak długo, jak zachcę,
pozwoli się podzielić na małe wieczności
pelne wstrzymanych v locie kul.
Na zawsze, jeśli każę, nic się tu nie stanie.
Bez mojej woli nawet liść nie spadnie
ani źdźbło się nie ugnie pod kropką kopytka.

Jest więc taki świat,
nad którym los sprawuję niezależny?
Czas, który wiążę łańcuchami znaków?
Istnenie na mój rozkaz nieustanne?

Radość pisania.
Możność utrwalania.
Zemstva ręki śmiertelnej.

(*Wisława Szymborska,* Radość pisania)

This is a poem of a Polish lady-poet Wislawa Szymborska, the Nobel laureate for poetry of 1996. Here is its English translation [15]:

(…)

The twinkling of an eye will take as long as I say,
and will, if I wish, divide into tiny eternities,
full of bullets stopped in mid-fight.
Not a thing will ever happen unless I say so.
Without my blessing, not a leaf will fall,
not a blade of grass will bend beneath the little hoof's full stop.

Is there then a world
where I rule absolutely on fate?
A time I bind with chains of signs?
An existence become endless at my bidding?

The joy of writing.
The power of preserving.
Revenge of a mortal hand.

(*Wisława Szymborska,* The joy of writing)

Prodigious, without limits, is the imaginative power of poetry. Is not this description of the „mortal hand", capable of creating any possible world and arresting it for never moving, assuring permanence of being, an impressive demonstration of human craving for immortality? – Which, as we biologists know, is nothing but a level-specific property of „selfish genes" that tend to preserve their continuance.

But there are other powers as well. Less illusory, more concrete ones. The power of politics, for instance.

In 1969, Murray Rabinowitz, an outstanding American specialist in the field of mitochondria, invited Piotr Slonimski to become Visiting Professor at the University of Chicago. In one summer evening, we met with Piotr at the campus. We sat down, with a bottle of wine, and spent almost the whole night in a long chatting. We took up many themes. It was there that I learned from Piotr that if he had not been a researcher, politics would have been his preference as profession.

For those who know the life path of Piotr, the importance he has ascribed to politics is of no surprise. The Second World War had molded him as a young man. Where else could he get a better lesson of how tremendous, and at the same time irrational, can be the power of politics than in his native Poland under the Nazi occupation? His father, a prominent Polish

scientist, zoologist and anatomist, did not survive the war – he perished in 1944 in Warsaw Uprising. Some of the relatives were killed in Auschwitz. Piotr´s uncle, Antoni Slonimski, a notable Polish poet survived – but only because he had emigrated in 1939, first to Paris and later to London. The illegal revolt against the Nazi occupants, this was Piotr´s first university, the imprinting one.

I guess that most of those who know Piotr more closely would concur that his unusually rich imagination is the imagination of a poet. Why, then, has he not become a poet, why did he not start to revenge on the world that had afflicted him so profoundly, by following the prescription of Szymborska? In 1949 the philosopher Theodor Adorno [1] voiced the famous assertion that one cannot write poetry after Auschwitz, at least not the same type of poetry as before. I would say that Piotr Slonimski might have been one of those poets who have paid heed to Adorno´s thesis. I don't know whether he has ever written a single poem in the old style. And yet, his all life work is in fact a homogenous, consistent, integral work of poetry. It is a poetry that has become science and a science that has become poetry. In what is Slonimski´science a new kind of poetry?

First, it is the poetry with no less power than is the creative power of the „mortal hand" of the poet Wislawa Szymborska. In contrast to the latter it is not an illusory power. It is the power that is inherent to scientific knowledge. And yet, the power of Slonimskí´s science is not the power of the science of Francis Bacon. Slonimski´s science does not aim at manipulation with Nature, at violating it, at forcing it to „excrete" technology. From what I know of Slonimski I dare say that the power of his science consists in harmony with which it is enriching individual human life, in freedom from ignorance, prejudices, mythology, in serenity in face of forces of nature and even more of social dynamics. It is in line with this conception of science that the man who was laying foundation for technological exploitation of yeast has not become an entrepreneur, has not entered the lucrative business as did many of those for whom science is everything else but not poetry.

There is still another power of science. It is due to perenniality of the scientific discovery. In one of his poem, entitled Exegi monumentum, Piotr´s uncle Antoni Slonimski meditates upon the temporariness, transience of human fame and of work of poetry. In science, things are different. Even though all truth of science is always preliminary, any scientific discovery, even the least one, is becoming a constituent of a single coherent edifice. Science is the only kind of poetry in which an actor is daily touching eternity.

Slonimski did not choose yeast as an object of his all-life research with regard to the fact that the organism is economically important. He did not intend to improve quality of

bread or beer. This is the second feature that makes of Slonimski´s work poetry. For Piotr Slonimski, a post-Auschwitz poet, yeast is – I would say – a metaphor of human. According to the definition of the Concise Oxford Dictionary, metaphor is the „application of name or descriptive term to an object to which it is not literally applicable". We may say that a metaphor is making an object familiar to us by simplifying it and accentuating its essential features. It has been customary to call yeast a „model organism". We ourselves have given the name to our Symposium „Yeast as a model for mitochondria-related human disorders".

They are some evolutionary biologists who oppose the term of a „model organism". There are mainly those who deny that biological evolution is progressing. They argue: why should yeast be a model of human; why not human be a model of yeast? However, the term is justified in two ways. If one omits the culturally imposed normative connotation, the word „progress" is left as a neutral, valueless expression of an evolutionary tendency. The tendency of evolution toward increasing complexity is undeniable. In evolution, thermodynamic depth is getting ever more profound [13], distance from thermodynamic equilibrium is getting larger [10], knowledge is increasing. Any evolutionary system is building upon what has been previously accomplished; evolution is a process of generative entrenchment [17]. This nature of evolutionary systems substantiates Delbrück´s principle of minimal complexity [10] that is of fundamental heuristic importance: The most efficient way to study a concrete biological phenomenon is by studying it on the simplest organism in which this phenomenon can be found – here it is experimentally best accessible and, because of its evolutionary simplicity, theoretically the most comprehensible.

We will have the opportunity to witness the validity of the principle here, at our symposium.

The second reason for using the term model is due to the fact that science is inevitably anthropocentric. As put by Popper [14], both amoeba and Einstein are exposing one's own hypotheses of the world to falsification, but science is a unique, human, species-specific way of falsification of hypotheses. On the other hand, abandoning the anthropocentric standpoint may be a revealing allegory. Let us look at the world through the „eyes" of a yeast, let us adopt a „zymocentric" standpoint. Yeast *S. cerevisiae* can consider itself as a very successful species. It can consider the environment of vineyards, breweries, bakeries and of research laboratories as its proper biological niche and can boast of its high fitness. In the view of a yeast philosopher humans may appear as a biological species that yeast has appropriately domesticated to assure its own biological success. Such an inversion of optics may not be an idle and naive exercise in would-be poetry. It indicates that in the boundless network of

causes and consequences in the world no description is possible without assuming a definite, largely arbitrary, standpoint, and focusing on any logical connections may be justified. We, humans, with our illusion of freedom of conscious action, are simply taking our natural, anthropocentric, standpoint.

There is a third feature that gives Slonimski´s work the character of poetry: it is the definitive form of the majority of publications he has been a co-author. It reminds the insurmountable restrictions that were determining the form of Russian orthodox icons. Slonimski´s powerful imagination rarely became unbridled to produce sweeping speculations. (I only recall two publications, which may be exceptions, apparently dominated by the second author, the poet of another type, Antoine Danchin [4], [5].) In publications with other co-authors Slonimski has made just a hint – dramatic just because being so tiny and provoking – that mitochondria may exhibit sex [2] or that the network of genes may resemble neuronal nets [6]. Just as the stern canon had imposed on an icon a stringent austerity that was only enhancing the hidden passion of its creator, the poetry of the publications from Slonimski´s laboratory carries a charm and elegance luring into extrapolations and fantasies.

Now, from a poet to a politician. Why Slonimski has not become a professional politician? Not only because he had been a Polish immigrant in the stern and selective French political environment. Practical politics may presuppose a different type of personality than is that of Piotr. From time immemorial, in human over-biological, hence political, groups power has been divided between the chieftains and the shamans, the former possessing political, the latter spiritual power. In grand politics Slonimski would be suited for being a shaman rather than a chieftain. This, however, does not hold for politics of science. Piotr Slonimski has been an outstanding politician of science, with a unique idiosyncrasy. As noticed by Krohn and Küpfers [11], science as a process is not only researching, but also an activity that they have called sciencing – all the organizational rush without which the pure researching would not be possible. More part of sciencing than of researching is the ability to find appropriate topics of research, in particular perceive the potential of a new discovery, to detect that somebody somewhere in the world has just uncovered a new mine, to get straight into the front line and to put to mining an effective team. The exquisite ability of Piotr to do this became probably most evident in the domain of analysis of the mitochondrial genome. The second half of the 1960s may have been a period of creative crisis at Gif. Yet, two publications in 1968 from Linnane´s [12] and Wilkie´s [16] laboratories on extranuclear heredity of antibiotic resistance were enough for Piotr to grasp immediately the far-reaching importance of the discovery. In the course of two years he put a concentrated effort to explore the new gold mine. In a

monumental publication from 1970, summarizing the imposing results of this effort, it has been stated in the Acknowledgement that the substantial part of work had been done by ´students of the „Diplôme d´Etudes Approfondies de Génetique“ des Facultés des Sciences de Paris et d´Orsay“, during their advanced training in the Laboratory in 1968 and 1969´ [3]. The latter fact, the major participation of students on research headed by Slonimski, is not to be overlooked. Teaching was an integral part of Piotr´science. He has been Professor of molecular genetics since 1966, but he had also taught genetics before this year. I dare say that the success of Piotr in science, but also his personal satisfaction, has been conditioned by his combining the two Krohn and Kűpfers´components of science with the third one. He may have proven a principle which we may call the principle of triunity (or trinity) of science: Integral science consists of three interrelated components: researching, sciencing, and teaching.

Tens, if not hundreds, are those who worked in Slonimski´s group, people from all over the world, who do consider themselves to be Piotr´ disciples. There may also be a large number of people who did not work directly at Gif, but do nevertheless acknowledge the formative influence of Slonimski upon their research. Many of them would be able to list domains of their research carrying the imprint of Slonimski´s way of thought. In the written abstract of my talk I have indicated how influential have been contacts with Piotr upon the work done in our laboratory. He has affected these lines of our research:

(1) Biochemical genetics of oxidative phosphorylation.

(2) Cooperation of nuclear and mitochondrial genes in biogenesis of mitochondria.

(3) Obligatory requirement of intramitochondrial ATP for normal functioning of the eukaryotic cell.

(4) Replication of telomere-equipped linear mitochondrial DNA.

(5) Interspecies transplacement of mitochondria.

(6) Cognitive biology.

It is this last domain of research that I am going to treat in the closing part of my talk. Piotr Slonimski has been an ambitious scientist, no doubt. But, as long as I could observe, there has been not a trace of vanity in his ambitions. Nothing would be more remote from his ambitions than an idle, empty panegyric. On the other hand, I believe that it may be gratifying for him to know that he has also affected a domain of research that may superficially appear to have no connection to yeast. Cognitive biology is linked to recent attempts at „naturalizing“ epistemology, commonly known under the name evolutionary epistemology [10]. The attempts strive to make of the nature of knowledge a biological problem, to consider life in its

entirety as a cognitive process and to conceive of biological evolution as the evolution of knowledge.

Incidentally, this has been a reason why some biologists, quite in conformity with Delbrück´s principle, have been using simple organisms, even bacteria, in research on cognition and behavior. The service rendered in these studies by bacteria has been so important that David Koshland, one of the pioneers of the use of bacteria in research on behavior, has put it plain in 1977 [9]: "A modern molecular biologist might paraphrase the poet Pope by saying, The proper study of mankind is the bacterium."

Yeasts have long competed with bacteria as model organisms in biology, in particular *S. cetevisiae* with *E. coli*. It is however, quite surprising that there has been one exception: In contradistinction to bacteria, yeasts have practically not been used in studies on behavior and cognition. There has been neglect here and it should be removed. Yeast, too, is a cognitive system. The yeast genome and proteome databases contain a number of data that are relevant for epistemology but have as yet been not subjected to a systematic analyses from this standpoint. I have listed here some problems with epistemological relevance that await more thorough studies:

(1) What is the reality of the yeast *Saccharomyces cerevisiae*, its internal model of the world?

(2) Does the network of genes and proteins resemble and model a neuronal net?

(3) In addition to chemical sensing („smelling" and „tasting") and mechanical sensing („touching") – osmosensing may be complemented by sensing of mechanical stretch and pressure – does yeast sense light and sound?

(4) Can pseudofilamentation of yeast colonies be oriented in space by imposed gradients and considered to be sort of exploration of the environment?

(5) What is the evolutionary path from translocators to sensors?

(6) Can mutants, typified by specific mutations in *snf3* and *rtg2* genes for glucose sensors that are signaling the presence of glucose in its absence, be considered as models of „molecular delusion"?

It may be in line with the analysis of Slonimski´s merit if we paraphrase Koshlad´s paraphrasing of Pope and make of the new paraphrase a new principle which may be called Slonimski´s principle: "A modern molecular biologist might paraphrase the poet Pope by saying, The proper study of mankind is the yeast."

Now, however: For how long may this dictum hold? It has surely held all the long Slonimski´ s professional career. The dazzling progress of yeast research is so quick that it

may take but a few years to be no longer of use. According to André Goffeau [7], who was referring to a personal communication from Jim Garrel and Peter Hodges, in the period of the last 4 years at least 5000 scientists in more than 1000 laboratories has published nearly 7000 papers on yeast genes and genomics. It may be estimated that in the early years of Piotr Slonimski´s carrier, shortly after the Second World War, the community of scientists in the entire world working on yeast as a model organism may have not been larger than a hundred of persons. The Golden Age of "zymology", optimistically foreseen by Mark Johnston [8], may turn to be a phantasm; the gold mine may soon be exhausted.

What will come next?

There exists a famous statement, ascribed to Claude Lévi-Strauss, the famous French ethnologist and Slonimski´s colleague in the French Academy of Sciences: "Le 21ème siècle sera le siècles des sciences humaines ou il ne sera pas." – "The 21st century will be the century of cultural (*i.e.* human and social) sciences or it will not be".

Perhaps the original saying of the poet Pope becomes effective, I am presenting it here in its original context:

This, however, will not contradict Slonimski´principle put up before. I am not sure whether Piotr would agree, but Pope's words, in combination with the statement of Lévi-Strauss, may still be Slonimski´s principle, but now valid for the 21st century. Although we are already in the 21st century, the validity may be postponed for a few years. Just enough for those of us who have come together today here to prove that yeasts continue to be a proper model for mitochondria-related human disorders. It is a pleasure to have Piotr Slonimski among us.

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