Simple Minds—Yeast as a Model Neuron

Isabella Sarto-Jackson[a], **Lubomir Tomaska**[b]

[a]Konrad Lorenz Institute for Evolution and Cognition Research,
Martinstrasse 12, 3400 Klosterneuburg, Austria
isabella.sarto-jackson@kli.ac.at
[b]Department of Genetics, Comenius University in Bratislava, Faculty of Natural Sciences,
Mlynská dolina, Ilkovičova 6, 842 15 Bratislava 4, Slovakia
lubomir.tomaska@uniba.sk

Abstract

Recent debates in cognitive science revolve around a core concept of cognition beyond an anthropocentric perspective. Researchers have aimed at recreating evolutionarily inspired solutions equivalent to nature-based faculties in organisms. By using model organisms, scientists have begun to formulate a consensus view on what might be called basal cognition based on nervous system of simple organisms like sea slugs, flies, and flat worms. Noteworthy, Koshland (1983) pioneered this idea and traced cognition down to the 'base' of the phylogenetic tree by emphasizing analogies of the bacterial chemosensory system and information processing to those in neurons of complex organisms. Taking up this idea, we have argued that evolutionary 'recent' specializations of the nervous system have adopted cellular processes that have derived from ancient and fundamental cell survival processes (Sarto-Jackson and Tomaska, 2016). We will provide arguments for using yeast as a model system of basal cognition to elucidate neuronal functions based on similarities in basic cellular architecture and homologies of molecular components.

1 Introduction

Although most behavioral and cognitive scientists agree on a core concept of cognition that involves processes like perception, learning, memory, and action, the biological phenomenon of cognition still remains highly elusive. Underlying bona fide cognitive skills is the individual's ability to process internal representations. Incontrovertibly, these skills are best exemplified by evolutionarily highly complex organisms, in particular humans. Following this line of thinking, refined human capabilities such as reasoning, problem-solving, and symbolic processing have become a benchmark for defining cognition. This conviction has led to a methodological and conceptual inclination to interpret cognition from an anthropocentric perspective. In this light, cognition is described as a rare commodity of extraordinary intrinsic complexity. To grapple with this complexity, cognitive scientists in the past have tackled cognitive processes by focusing their domains of study on vertical microworlds, i.e., by decomposing their research agenda and studying small slices of human-level cognitive competence (Clark 1989). As a consequence, researchers have come up with technically sophisticated and cleverly designed solutions to evolutionarily recent, anthropocentric problems. These solutions, however, may significantly differ from natural solutions as the former usually do not take the evolutionary history of such cognitive tasks into account. Instead, their central aim is to solve the cognitive task at issue rather than recreating evolutionarily inspired solutions equivalent to nature-based faculties in organisms.

2 The concept of basal cognition

Over the last few decades, however, research approaches in cognitive science have become more encompassing. Researchers have increasingly turned their attention to horizontal microworlds that mimic the complete behavioral competence of whole creatures (Clark 1989). In this vein, cognition is understood as the evolution-derived capacity of sensory and other information-processing mechanisms an organism exhibits in order to evaluate and interact with its internal milieu and with challenges encountered in its environment. Scientists have thus begun to look beyond the anthropocentric interpretation of cognition by using model organisms such as primates and other mammals, and even invertebrates like sea slugs, flies, and flat worms. What has been almost entirely missing in this broadened dialogue, however, is an understanding of what might be called basal cognition, i.e., cognition at the 'base' of the phylogenetic tree. Discarded as evolutionarily outmoded ways of information processing, this ground floor of organismal complexity — as found for example in single cell organisms that lack any nervous system — has been viewed as irrelevant for understanding the phenomenon of cognition. The first scholar who challenged this belief and offered thought-provoking arguments about the analogies of the bacterial chemosensory system and information processing in neurons of complex organisms was Koshland (1983). He emphasized that bacteria continually monitor their external and internal environments and compute functional outputs based on information provided by the sensory apparatus. Since then, more and more researchers have argued that cognition has first and foremost evolved to enable organisms to control their own behavior in order to cope with such internal (van Duijn et al. 2006) and environmental complexities (Godfrey-Smith 2002). In this sense, cognition represents an organism's existential needs for survival, growth, and reproduction. By extrapolation, it can be assumed that different taxa will have varying cognitive toolkits relative to their stage of biological organization. This line of thinking allows for a conceptual refinement of the wide array of cognitive capabilities that can be found in nature. At the basis of this assumption lies the notion of minimal cognition. This endeavor aims at articulating minimal requirements for the generation of cognitive phenomena. It thereby challenges the view of restricting the definition of cognition to solely higher-level cognitive skills in anthropocentric terms and recognizes single cells organism as sentient beings.

By studying single cell organisms, problems of human-level intelligence can be simplified without losing track of the basic biological principles of information processing including real-time responses, integration of motor and sensory functions, and mechanisms for intercellular communication. This approach provides a rational for grappling with the increasing sophistication of most complex, multi-faceted biological functions by means of comparative studies of different types of organisms. This comparative approach is based on the assumption that there exists a meaningful degree of continuity among these organisms and cognitive phenomena are subject to evolutionary tinkering. Starting with the smallest, simplest potential example of signaling processes in single cell organisms, it should be possible to derive basic principles of cognition. In more detail, elucidating crucial components of information processing can contribute to understanding homologous mechanisms of inherited cellular and organismal behavior according to their evolutionary trajectories. For example, cognition depends upon the processing of information by protein molecules operating in circuits. Neurons process information chemically, electrically and mechanically because of their capacity to exploit the adaptability of their cellular proteins, the specificity of their interactions, and their ability to construct circuits. This processing capacity is, in turn, constrained by the mathematics of information, thermodynamics, protein kinetics, cell biology and the cost of space, materials and energy. Consequently, information processing must have been shaped by physical, chemical and phylogenetic constraints thereby driving the evolution of cognition — be it in neurons or single cell organisms. This line of thinking strongly supports the research program of cognitive biology that aims at synthesizing insights from different scientific disciplines within a single framework. According to cognitive biology, biological evolution as a whole can be understood as the evolution of cognition (Kováč 2000; 2006). Conceptually, it "adheres to a principle of minimal complexity (i.e. Delbrück's principle), which stipulates that the most effective way to study any trait of life is by studying it at the simplest level at which it occurs" (Kováč 2005, p S15).

This is in excellent agreement with Koshland's seminal paper (1983). There, Koshland convincingly argued that bacteria use cellular mechanisms to modify incoming signals in order to produce functional plasticity resulting in behavioral plasticity. Despite additional important work on cognitive processing in bacteria in the recent past (van Duijn 2006; Lyon 2015; Lyon 2017; Pinto 2016), several important challenges remain unaddressed. Some of these unaddressed challenges stem from the fact that bacterial model organisms can hardly be exploited to investigate how signaling cascades lead to structural plasticity, either by changing cell morphology per se or by generating intercellular communication networks1. Elucidating pathways and components involved in this type of phenotypic plasticity are, however, among of the most pressing endeavors in cognitive science and neurobiology. This is due to the fact that specific neuronal functions are intrinsically intertwined with the morphological characteristics of distinctively polarized cells. Neurons harbor specialized protrusions that enable them to precisely transmit intercellular signals as well as integrate and propagate information in the form of electrical potentials. While the combined appearance of these key characteristics of morphological and functional specialization is unique to the nervous system of metazoan animals, many of these functional as well as structural features can be found in non-nervous cells including yeast.

3 Yeast as a model neuron

Taking up this idea in a recent paper, we have argued that evolutionary 'recent' specializations of the nervous system have adopted cellular processes that have derived from ancient and fundamental cell survival processes (Sarto-Jackson and Tomaska, 2016). For example, many components underlying signal propagation, cell morphology, or cell-cell communication are evolutionary conserved between yeast and higher eukaryotes. Given the fact that yeast cells are unrivalled by means of detailed scientific knowledge about their metabolism, signal

---

[1] With the exception of most recent studies concerning quorum sensing in bacteria.

transduction, cell division, morphogenesis, genetic and protein interaction networks, it makes them excellent model organism for issues of investigations of the cognitive realm.

Using examples of (1) polarization processes and (2) cell-cell communication, we will show similarities in responsiveness to highly selective stimuli derived from putative interaction partners. By means of these examples, we will map the general outlines of the domain of basal cognition from unicellular eukaryotes (yeast) to neuronal cells of the animal nervous systems. This will allow tracing of biological mechanisms necessary for implementing a cognitive toolkit of behavior-generating capacities. In this comparative approach, we will mainly focus on conserved mechanisms that have been exploited by evolution and can thus also be found in systems that possess much more complex biological organization.

(1) Polarization

Neurons usually develop polarity by redistributing proteins and lipids in response to either external or intrinsic cues that then lead to distinct morphological changes. The process of cellular polarization is characterized by three stages: symmetry breaking, directional sensing, and motility. Yeast cells exhibit polarization responses during budding in vegetative growth as well as during mating between haploid cells of opposing mating types or during filamentous growth upon nutrient deprivation. While the former can occur spontaneously without the necessity of an external directional cue, the latter two require cues in the environment. Neurons undergo polarization during neuronal migration and maturation, neurite outgrowth of mature neurons as well as during spine formation. These structural specifications are of paramount importance for subsequent network formation underlying signal transmission and neuronal communication, broadly conceived. Crucial for cellular asymmetries in neurons are external cues that trigger structural changes and shape the overall morphology. In both types of cells, yeast and neurons, the balanced activity of signaling molecules and molecular sensors induce different cell morphologies and trigger the recruitment of evolutionarily homologous proteins and downstream effectors. These conserved proteins give rise to comparable subcellular processes, yet the specific behavioral outputs differ due to constraint of species-specific biorealities (Gontier and Bradie 2018).

(2) Cell-cell communication

The nervous system of a multicellular organism represents an intricate network of neurons. Importantly, the wiring diagrams of complex neural systems are by no means pre-programmed nor do they follow a fixed pattern of connectivity. On the contrary, synaptic connections between neurons undergo constant remodeling and changes. These modifications manifest themselves in specific neuroplastic events that are executed through distinct signaling pathways. Neurons persistently receive signals from the environment or adjacent cells and must convert these signals into an appropriate reaction inside the cell by signal transduction. It may be counterintuitive to use unicellular organisms such as yeast in order to understand biological features of dynamic network formations. However, in contrast to general assumptions, yeast cells do not display fully predictive, inflexible, and hard-wired reactions to environmental cues. Mathematical models have shown that their reaction patterns are more likely to be probabilistic rather than strictly deterministic. In addition, yeast cells can undergo extensive morphological changes upon stress, such as switching to pseudohyphal growth or invasive growth (depending on their genotype). For these growth processes to occur, signals from nutrients and metabolic by-products must be integrated. This summation process causes physical responses that alter adhesion, budding polarity, morphology and cell cycle control of individual cells organizing the growing cells into structured networks. Intriguingly, both, microbial growth and cell-cell contacts in multicellular organism (in neuronal tissue as well as synapse formation) strongly rely on self-recognition processes via cell adhesion molecules. Thus, yeast cells and neurons share surprisingly comparable morphological and molecular features with respect to cell polarization, elongated cellular morphology, and homotypic cell-cell contact.

4 Conclusion

In summary, we will provide a number of examples demonstrating that studying yeast brings numerous benefits for a better understanding of neurons. Due to similarities in their basic cellular architecture and homologies of molecular components, both, yeast and neurons solve various problems associated with cellular life by using evolutionarily adaptive, analogous molecular logic. In addition, the rich social life full of intricate (direct and indirect) intercellular contacts of yeast cells will give further insights that may help in elucidating "the wiring diagram of complex neural systems."

References

Clark, A. (1989). *Microcognition*. Cambridge, MA: MIT Press.

Godfrey-Smith, P. (2002). Environmental complexity, signal detection, and the evolution of cognition. In: M. Bekoff, C. Allen & G. Burghardt (Eds.) *The cognitive animal: empirical and theoretical perspectives on animal cognition* (pp. 135-141). Cambridge, MA and London: MIT Press/Bradford Book.

Gontier, N., & Bradie, M. (2018). Acquiring knowledge on species-specific biorealities: The applied evolutionary epistemological approach. In R. Joyce (Ed), *The Routledge Handbook of Evolution and Philosophy* (pp. 136–155) New York, NY: Routledge.

Koshland, D.E. Jr., (1983). The bacterium as a model neuron. *Trends in Neuroscience, 6*, 133–137.

Kovac, L. (2000). Fundamental principles of cognitive biology. *Evolution and Cognition, 6*, 51–69.

Kovac, L. (2006). Life, chemistry and cognition. *EMBO Reports, 7*(6), 562–566.

Kováč L. (2006). Life, chemistry and cognition: Conceiving life as knowledge embodied in sentient chemical systems might provide new insights into the nature of cognition. *EMBO Report, 7*, 562–567.

Lyon, P. (2015). The cognitive cell: bacterial behavior reconsidered. *Frontiers in Microbiology, 6*, 264.

Lyon, P. (2017). Environmental complexity, adaptability and bacterial cognition: Godfrey-Smith's hypothesis under the microscope. *Biology & Philosophy, 32*, 443-465.

Pinto, D., & Mascher T. (2016). (Actino)Bacterial "intelligence": using comparative genomics to unravel the information processing capacities of microbes. *Current Genetics, 62*, 487–498

Sarto-Jackson, I., & Tomaska, L. (2016). How to bake a brain: yeast as a model neuron. *Current Genetics, 62*, 347–370.

Van Duijn, M., Keijzer, F., & Franken, D. (2006). Principles of minimal cognition: Casting cognition as sensorimotor coordination. *Adaptive Behavior, 14*, 157–170.