37th ALTENBERG WORKSHOP IN THEORETICAL BIOLOGY

The Ground Floor of Cognition: From Microbes to Plants and Animals

organized by

Pamela Lyon and Fred Keijzer

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KLI, Klosterneuburg

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Welcome

to the 37th Altenberg Workshop in Theoretical Biology. The Altenberg Workshops are interdisciplinary meetings organized by the KLI in Klosterneuburg, Austria. The workshop themes are selected for their potential impact on the advancement of biological theory. Leading experts in their fields are asked to invite a group of internationally recognized scientists for three days of open discussion in a relaxed atmosphere. By this procedure the KLI intends to generate new conceptual advances and research initiatives in the biosciences. We are delighted that you are able to participate in this workshop, and we wish you a productive and enjoyable stay.

Gerd B. Müller
President

The topic

The cognitive domain and its relation to behavior is labyrinthine and obscure, despite remarkable advances in molecular imaging, genetics and *in vivo* measuring techniques. Thus, we still know very little about how cognition works in lived life, even when the myriad connections between neurons effectively have been mapped, as they have been for the model organism *Caenorhabditis elegans*. Elevating the level of difficulty is the fact that we are trying to plumb the depths of the most complex, multi-faceted biological function we know of with one hand tied behind our backs.

How? Because those who study cognition have yet to avail themselves of the most successful methodology in the life sciences: start with the smallest, simplest potential example of the function or mechanism, derive basic principles, and then test in increasingly complex organisms. This is how the greatest advances in the biological sciences have been achieved, from understanding the mechanisms of inheritance to the intracellular production and behavior of proteins to the operation of ion channels.

What is almost entirely missing is an understanding of what we might call *basal cognition*, cognition at the 'base'—the ground floor—and lower branches of the tree of life, from the simplest organisms to the origin(s) of nervous systems. Among the obstacles blocking the path to understanding are two traditional, arguably outmoded ways of thinking. First is Lamarck's criterion that the ascription of cognitive capacity requires a nervous system of 'sufficient complexity'. Second is the view that prokaryotes and eukaryotes are separated by a largely insuperable 'phylogenetic dike'.[1] As a result of these for the most part unquestioned dogmas, relatively few have bothered to look beyond these barriers, barriers which for most of the life of the modern cognitive sciences tended to discount even relatively complex organisms, such as insects and other small invertebrates.

Our project, then, is to map the general outlines of the domain of basal cognition, from prokaryotes (principally bacteria) and unicellular eukaryotes, to plants and simple animals without and with nervous systems. This will involve tracing, to the extent possible, the biological mechanisms necessary for implementing a cognitive toolkit of behavior-generating capacities—for example, sensing, memory, learning, decision making, anticipation, and communication—noting where mechanisms are conserved and where they diverge as more complex biological organization evolves.

An important facet of exploring basal cognition, often lost in the study of brain-based cognition, is the inescapable reality that cognitive capacities such as sensing, memory, problem solving, anticipation and so on are, in the life of an organism, first *focused inward*, on constructing and maintaining the anatomy needed to make a living in an environment. Cognitive capacities therefore necessarily will (in Godfrey-Smith's terms) 'shade off' into other biological functions. This dependence is present in all organisms, but at the level of basal cognition it is abundantly clear.

Because so many discussions of cognition often degenerate into semantic arguments over what the term means—which is why no scientific (to say nothing of philosophical) consensus exists to this day—we will be clear about the preliminary definition we are adopting for our discussions:

> *Cognition is the complex of sensory and other information-processing mechanisms an organism has for becoming familiar with, valuing, and interacting with its internal milieu and with features of its environment in order to meet existential needs, the most basic of which are survival/persistence, growth/thriving, and reproduction.*

Of the many challenges facing this task the greatest barrier is a highly disparate and incomplete literature relating to the different capacities in the cognitive toolkit relative to varying taxa. Thus, if we concentrate solely on the individual capacities in the cognitive toolkit, at the different stages of biological organization, we will quickly run up against gaping holes in the experimental literature.

One way we will attempt to work around this difficulty is by concentrating on a single, albeit multi-faceted cognitive capacity: *decision-making*. Decision-making requires almost the entire cognitive toolkit: physiological (internal) and environmental (external) sensing; memory; some means of integrating information from different sources; some capacity for placing a value on that information relative to existential imperatives; and cell-cell communication. The mechanisms and how they interact within the organism may not be well-understood, but the capacity to decide between one course of action and another, and/or to correct course following negative feedback or significant perturbation, is evident in all living things.

By focusing on decision-making, and the molecular mechanisms involved (how, we may not yet know), we conceivably will be able to link basal cognition and its evolution more straight-forwardly to the science of cognition-without-caveats.

[1] Kennelly, P.J. and M. Potts (1996). Fancy meeting you here! A fresh look at 'prokaryotic' protein phosphorylation. *Journal of Bacteriology* 178(16): 4759-4764.

Format

There will be 15 presentations, with 45 minutes allotted for each—roughly 30 minutes for each talk, followed by 15 minutes for Q&A and discussion. On Friday we will begin with a short welcome and introduction by the organizers, addressing the aims and framework of the workshop, and end with a general stock-taking session. Saturday is a full day of eight (8) presentations. On Sunday we end with a general discussion, including publication plans.

Manuscript preparation and publication

The Altenberg Workshops in Theoretical Biology are fully sponsored by the KLI. In turn, the KLI requests that all participants contribute to a volume edited by the organizers. The results of Altenberg Workshops are usually published in the *Vienna Series in Theoretical Biology* (MIT Press).

From the beginning, our collective approach to this work has been quite different to the typical Altenberg Workshop volume. Curated collections of essays under a central theme, which are customary from specialist conferences, including in the KLI series, undoubtedly move the knowledge enterprise forward in important ways. However, their shelf-life can be limited, and they are difficult to revise.

In the case of The Ground Floor of Cognition Workshop, we are all very aware that we are endeavoring to define the initial boundaries of a new field. Therefore, the aim is to develop and refine the insights gained at the workshop into an easy-to-use, multidisciplinary manual, or 'field guide,' to basal cognition.

Entries will tend to be shorter, and more digestible. Each participant will produce more than one entry. Most will produce text within the usual 8,000-10,000 word limit for an essay, while others may produce more, and a few perhaps less. Given this more expansive aim, the contributors to this volume cannot be limited to the original participants. Contributions will be invited from additional experts and co-authors by all of the participants, both inside and outside their respective fields, not only with the approval of the editors but also the group more generally. Several experts, who were unable to attend the Workshop, have already expressed their desire to be part of this larger project.

Finally, a high premium will be placed on graphic elements (e.g., diagrams, charts, drawings and other images). Anna Zeligowski, MD, who has now produced illustrations for four (4) MIT Press volumes to date, including one in the Vienna Series, will be providing illustrations to this field guide as well.

The hope is that, should it prove beneficial, the manual/field-guide will be capable of revision in the future, if not by us, then by others.

Pamela Lyon and Fred Keijzer

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The Ground Floor of Cognition: From Microbes to Plants and Animals

Thursday 14 June	Evening		
6.00 pm – 9.00 pm		Welcome reception (cold food provided) at the KLI	

Friday 15 June	Morning		Chair: Jablonka
9.30 am – 9.45 am	P. Lyon & F. Keijzer	Welcome Address & Introduction	
9.45 am – 10:30 am	Pamela Lyon	Basal Cognition: Filling in a Darwinian Jigsaw	
10.30 am – 11.00 am	Coffee		
11.00 am – 11.45 am	Simon Laughlin	Have Constraints on Protein Circuits Shaped the Evolution of Cognition?	
11.45 am – 12:30 pm	Bill Bechtel	Decision-Making: Heterarchical Control of Endogenously Active Biological Mechanisms	
12.30 am – 2.30 pm	Lunch	at the KLI	

Friday 15 June	Afternoon		Chair: Lyon
2.30 pm – 3.15 pm	Daniela Pinto	Signal Transduction in Bacteria: The Special Case of Alternative Sigma Factors	
3.15 pm – 4.00 pm	Pauline Schaap	Cell Signaling in Dictyostelid Social Amoebas and Its Evolution from a Unicellular Stress Response	
4.00 pm – 4.30 pm	Coffee		
4.30 pm – 5.15 pm	Audrey Dussutour	Learning in Slime Molds	
5:15 pm – 6.00pm		General Discussion: Lessons from Day One	
6.00 pm		Departure for Dinner to a local *Heurigen*	

Saturday 16 June	Morning		Chair: Keijzer
9.45 am – 10.30 am	Peter Godfrey-Smith	Minimal Cognition, Proto-Subjectivity, and Other Perplexities	
10.30 am – 11.15 am	Pawel Burkhardt	Origin and Evolution of Synaptic Proteins	
11.15 am – 11.45 pm	Coffee		
11.45 am – 12.30 pm	Frantisek Baluska	Plant Cognition and Behavior	
12.30 pm – 2.30 pm	Lunch	at the KLI	

Saturday 16 June	Afternoon		Chair: Schaap
2.30 pm – 3.15 pm	Fred Keijzer	On the Origin of Subjects	
3.15 pm – 4.00 pm	Argyris Arnellos	Individuality and Cognition: An Organizational Story of Co-Evolution	
4.00 pm – 4.30 pm	Coffee		
4.30 pm – 5.15 pm	Gáspár Jékely	Peptidergic Signaling at the Origin of Nervous Systems	
5.15 pm – 6.00 pm	Michael Levin	What Do Bodies Think About? Bioelectric Basis of Somatic Primitive Cognition in Embryogenesis, Regeneration, and Cancer	
6.15 pm		Free evening	

Sunday 17 June	Morning		Chair: Levin
9.45 am – 10.30 am	Detlev Arendt	The Origin of Central Nervous Systems	
10.30 am – 11.00 am	Coffee		
11.00 am – 11.45 am	Eva Jablonka	From Cognition to Consciousness: The Learning Route	
11.45 am – 12.30 pm		General Discussion & Publication Plans	
12.30 pm – 2.15 pm	Lunch	at the KLI	
2.30 pm		Departure for Danube boat trip and dinner at Schloß Dürnstein	

Abstracts

Pamela LYON
Flinders University of South Australia

Basal Cognition: Filling in a Darwinian Jigsaw

One of Darwin's more radical intuitions was that, in a very broad sense, the differences between organisms, 'mental' as well as physical, are principally ones of degree but not of kind, due to their probable common origin in a unicellular organism and taking into consideration common requirements for staying alive. Darwin himself was not entirely clear what he meant by this, but the fact that he was concerned elsewhere with 'emotions in earthworms'—and this in the 19th century—suggests his intuitions lodged at the 'stronger' end of what Godfrey-Smith calls the *continuity thesis*, the recognition that life and cognition are co-extensive to a degree that currently remains a matter of personal philosophical preference rather than scientific demonstration.

In defense of a strong continuity thesis, here I will present recent empirical evidence that phenomena uncontroversially associated with cognition in more complex animals are found in prokaryotes, notably bacteria, and sometimes are implemented by similar or the same mechanisms. I will highlight the roles of following phenomena involved in generating complex bacterial behavior: 1) protein networks; 2) stress responses; 3) hormone-like autoinducers involved in coordinating changes in gene expression within a cell population to alter cellular phenotype; 4) electrical signaling mediated by ion channels for transducing signals across large numbers of cells; 5) bacterial (rhod)opsins that respond to light; and 6) myxococcal swarming motility, which rely on cell-cell contact, transient adhesion, and a bacterial homologue of actin.

Biographical note:

Pamela Lyon is a natural philosopher concerned with the characterization and *evolution of cognition as a biological phenomenon* (Lyon 2006). Her work to date has been primarily *grounded in microbiology* (Lyon 2015). She is currently working with Daniela Pinto on developing an 'adaptability index' (Lyon 2017), which would allow microbiologists to identify potentially behaviorally complex microbes from their genome sequence. Her main interest is the *co-evolution of cognition and biological responses to stress*, from bacteria to humans (Lyon et al. 2011; Lyon 2014).

Lyon P. (2006). The biogenic approach to cognition. *Cognitive Processing*, *7*(1), 11-29.

Lyon P. (2014). Stress in mind: A stress response hypothesis of cognitive evolution. In: L.R. Caporael, J.R. Griesemer, and W.C. Wimsatt (Eds.) *Developing Scaffolds in Evolution, Culture, and Cognition* (pp. 171-190). Cambridge, MA: MIT Press.

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.

Lyon P., Cohen M., and Quintner J. (2011). An evolutionary stress response hypothesis of chronic widespread pain (fibromyalgia). *Pain Medicine,* 12**,** 1167-1178.

Simon LAUGHLIN

University of Cambridge

Have Constraints on Protein Circuits Shaped the Evolution of Cognition?

Cognition depends upon the processing of information by protein molecules operating in circuits. The adaptability of proteins, the specificity of their interactions, and the ability of cells to construct circuits, molecule by molecule, offers huge opportunities to process information chemically, electrically and mechanically. Work on neurons shows how processing is constrained by the mathematics of information, thermodynamics, protein kinetics, cell biology and the cost of space, materials and energy. The efficient designs adopted by neurons indicate that these physical, chemical and phylogenetic constraints have shaped the evolution of cognition.

Biographical note:

Simon Laughlin is a neurobiological pioneer in the study of metabolic *constraints on neural organization and evolution* (Laughlin et al., 1998). These include the trade-off between chemical and electrical signaling, the role of *neuromodulation*, having and minimizing *neural wiring* and so on (see, e.g., Laughlin and Sejnowski 2003). He is co-author of *The Principles of Neural Design* (Sterling and Laughlin 2015). A member of the multidisciplinary collaboration that initiated the integrative study of work in living systems and co-author of the ground-breaking *Work Meets Life* (R. Levin et al. 2011), Simon is concerned with the energetic economy of neural function and the intrinsic connection between the neural control of behavior and physiology (Laughlin 2011).

Laughlin S.B. (2011). Energy, information and the work of the brain. In: R. Levin, S. Laughlin, C. De La Rocha and A. Blackwell (Eds.), *Work Meets Life: Exploring the Integrative Study of Work in Living Systems* (pp. 39-67). Cambridge, MA: MIT Press.

Laughlin S.B. de Ruyter van Steveninck R.R., and Anderson J.C. (1998). The metabolic cost of neural information. *Nature Reviews Neuroscience, 1*, 36-41.

Laughlin S.B. and Sejnowski T. (2003). Communication in neuronal networks. *Science, 301*(5641), 1870-1874.

Levin R., Laughlin S., De La Rocha C., and Blackwell A. (Eds.) (2011). *Work Meets Life: Exploring the Integrative Study of Work in Living Systems.* Cambridge, MA: MIT Press.

Sterling P. and Laughlin S.P. (2015). *Principles of Neural Design*. Cambridge, MA: MIT Press.

Bill BECHTEL

University of California, San Diego

Decision Making: Heterarchical Control of Endogenously Active Biological Mechanisms

Biological organisms are characterized by their ability to do things that serve to maintain their own continued existence, both individually and as parts of lineages. In particular, they take up matter and energy and put them to use in building, repairing, and replicating themselves. These capacities are achieved through a host of special-purpose *productive mechanisms* that are endogenously active: provided a source of energy, they are organized to carry out their tasks. To be effective in maintaining the organism, these mechanisms must be controlled so that they perform their tasks only when and in the fashion needed for the organism to survive or replicate.

Control has not played a central role in the philosophical discussion of mechanisms; accommodating it requires a revised conception of mechanisms as consisting of constraints that direct flows of free energy into the performance of work. Control mechanisms perform work to alter flexible constraints so that productive mechanisms, and hence the organism, perform different activities. For this to be done in a way that serves the needs of the organisms, control mechanisms require information procured by performing measurements.

Control mechanisms are organized so as to use this information to make decisions between different possible activities in productive mechanisms. *Procuring information and using it to make decisions is a fundamental cognitive activity*. To illustrate this perspective, I consider briefly examples of decision-making performed by control mechanisms in bacteria, slime molds, worms, and leeches. One might criticize such control mechanisms as too simple for cognition since they do not obviously involve internal processes that can maintain representations (and misrepresentations) of conditions in the organism's internal or external environment.

To examine how this is possible even without neurons, I focus on *circadian rhythms* that are maintained through *internal oscillatory mechanisms* whose phase stands in for time of day in the organism's environment. Even in organisms with neurons, the core circadian mechanism is intracellular. I will focus in particular on the circadian clock in cyanobacteria and show how it represents external time even when not receiving sensory inputs, is entrained by such inputs, and effects decisions about the operation of other mechanisms in the bacterium.

Considering the relation between circadian and other control mechanisms brings out another feature of control in living mechanisms—circadian control is just one form of control operating on productive mechanisms in biological organisms. Far from being organized into a neat hierarchy, even in relatively simple organisms, multiple control mechanisms operate on the same primary mechanisms, and control is realized through a *highly integrated, heterarchical, network* of control mechanisms.

Biographical note:

William (Bill) Bechtel is a philosopher who has spent most of his heterodox career at the forefront of *theoretical cognitive science* (Bechtel 1988, Bechtel et al. 1998, Bechtel 2013), latterly focusing on cognition's biological underpinnings (Bechtel 2014). Drawing on long interest in the history of *cell biology*, he helped to found the influential turn toward *mechanistic explanation* in the philosophical explication of how the life sciences explain phenomena (Bechtel 2008). Other research interests include *circadian rhythms* and *computational modelling* of biological phenomena.

Bechtel W. (1988). *Philosophy of mind: an overview for cognitive science*. Hillsdale, NJ: Lawrence Erlbaum Associates.
Bechtel W. (2008). *Mental mechanisms: philosophical perspectives on cognitive neuroscience*. New York: Lawrence Erlbaum Associates.

Bechtel W. (2013). The endogenously active brain: the need for an alternative cognitive architecture. *Philosophia Scientiae: Travaux d'Histoire des Sciences et de Philosophie, 17*, 3-30.
Bechtel W., Abrahamsen A., and Graham G. (1998). The life of cognitive science. In: W. Bechtel and G. Graham (Eds.), *A Companion to Cognitive Science* (pp. 1-104). Malden, MA and Oxford: Blackwell Publishers.
Bechtel W. (2014). Cognitive biology: surprising model organisms for cognitive science. *Proceedings of the 36th Annual Conference of the Cognitive Science Society: Cognitive Science Society*, 158-163.

Daniela PINTO

Technische Universität Dresden

Signal Transduction in Bacteria: The Special Case of Alternative Sigma Factors

Bacteria are traditionally considered simple life forms that are incapable of complex behavior, which is usually regarded as an exclusive trait of higher life forms. However, over the last decades an increasing amount of evidence contradicts this view. Signaling is the ground floor of such cognitive behavior, and at a molecular level it can be reduced to only a handful of mechanisms. Here, I will systematize current knowledge on the three fundamental mechanisms of signal transduction in bacteria with a special focus on the new developments in the field of 'alternative' sigma factors. Extracytoplasmic function sigma factors (ECFs) are transcription factors normally held in check, but are able to sense and respond to environmental signals. I will highlight the similarities and differences between signaling mechanisms described for bacteria and eukaryotes, and exemplify the potential and limitations of comparative genomics analysis to reveal bacteria's cognitive potential.

Biographical note:

Daniela Pinto is a microbiologist currently working on the genetics and comparative genomics of *bacterial adaptation to environmental stress* (e.g., Pinto et al. 2013; Kleine 2017), but is moving into the study of bacterial memory and learning. She has a keen interest in *signal transduction* (Huang et al. 2015), in particular *extracytoplasmic function (alternative) sigma factors* (ECFs) (Pinto and Mascher 2016a; 2016b), the so-called 'third pillar' of bacterial signal transduction. ECFs are transcription factors normally held in check but able to sense and respond to environmental signals. Although still poorly understood, ECFs are thought to increase the flexibility of a cell's behavioral options as conditions change.

Huang X., Pinto D., Fritz G., and Mascher T. (2015). Environmental sensing in actinobacteria: a comprehensive survey on the signaling capacity of this phylum. *Journal of Bacteriology, 197*, 2517-2535.

Kleine B., Chattopadhyay A., Polen T., Pinto D., et al. (2017). The three-component system EsrISR regulates a cell envelope stress response in *Corynebacterium glutamicum*. *Molecular Microbiology, 106*, 719-741.

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

Pinto D., and Mascher T. (2016b). The ECF classification: a phylogenetic reflection of the regulatory diversity in the extracytoplasmic function σ factor protein family. In: F.J. de Bruijn (Ed.), *Stress and environmental regulation of gene expression and adaptation in bacteria.* Wiley Online Library. John Wiley & Sons. Chapter 2.6.

Pinto D., Santos M.A., and Chambel L. (2013). Thirty years of viable but nonculturable state research: unsolved molecular mechanisms. *Critical Reviews in Microbiology,* 41, 61-76.

Pauline SCHAAP

University of Dundee

Cell Signaling in Dictyostelid Social Amoebas and Its Evolution From a Unicellular Stress Response

I will present an overview of the cell signaling networks that control aggregation, post-aggregative morphogenesis and cell type specialization in the model social amoeba *Dictyostelium discoideum*, and discuss conservation and change in signaling genes that control the *D. discoideum* developmental program across social amoebas and related unicellular species. Gene knockout and gene replacement studies provide evidence of how the control of aggregation, morphogenesis and terminal spore and stalk cell differentiation gradually evolved from a stress response in the unicellular ancestor. Comparative analysis of gene families involved in signal detection and processing across uni- and multicellular amoebozoa show that unicellular forms have a larger number and greater variety of cell signaling proteins than the social amoebas.

Biographical note:

Pauline Schaap is a developmental biologist known for her work in the genetics, functional mechanisms and evolution of aggregative multicellularity in social amoeba (Schaap, 2016; Schaap et al., 2016). She uses *evolutionary reconstructions and comparative genomics* to trace how the signaling capacities of the Dictyostelia evolved to enable development of motile multicellular slugs and (anchored) fruiting bodies via complex forms of cell-cell communication (e.g., Sucgang et al., 2011; Du et al., 2015; Glöckner et al., 2016). She is also interested in the evolutionary relations of *developmental signaling systems* among eukaryotes and prokaryotes (Schaap et al., 2016).

Du Q. et al. (2015). The evolution of aggregative multicellularity and cell–cell communication in the Dictyostelia. *Journal of Molecular Biology, 427***,** 3722-3733.

Glöckner G. et al. (2016). The multicellularity genes of dictyostelid social amoebas. *Nature Communications, 7***,** 12085.

Schaap P. (2016). Evolution of developmental signalling in Dictyostelid social amoebas. *Current Opinion in Genetics & Development*, *39***,** 29-34.

Schaap P. et al. (2016). The *Physarum polycephalum* genome reveals extensive use of prokaryotic two-component and metazoan-type tyrosine kinase signaling. *Genome Biology and Evolution, 8*(1), 109-125.

Sucgang R. et al. (2011). Comparative genomics of the social amoebae *Dictyostelium discoideum* and *Dictyostelium purpureum*. *Genome Biology, 12*(2).

Audrey DUSSUTOUR

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Learning in Slime Molds

Learning, defined as a change in behavior evoked by experience, has hitherto been investigated almost exclusively in multicellular neural organisms. Evidence for learning in non-neural multicellular organisms is scant, and only a few unequivocal reports of learning have been described in single-celled organisms. In the first part of this seminar I will demonstrate habituation, an unmistakable form of learning, in the non-neural organism *Physarum polycephalum*. In the second part, I will show that learned information can be transferred from one cell to another via cell fusion. Our results point to the diversity of organisms lacking neurons that likely display a hitherto unrecognized capacity for learning, and suggest that slime molds may be an ideal model system in which to investigate fundamental mechanisms underlying basal cognition.

Biographical note:

Audrey Dussutour is a biologist specializing in collective animal behavior and cognition. She studies *collective decision-making* working mostly on acellular slime molds (i.e., *Physarum polycephalum*) and ants (Dussutour and Simpson, 2009; Dussutour et al. 2010; Jeanson et al. 2012). While both systems are very different, they each exhibit interesting forms of decision-making strategies that capitalize on inter-individual variability and emergent forms of plasticity. Recent work includes habituation learning in slime molds (Boisseau et al. 2016), and the transfer of such learning via cell fusion (Vogel and Dussutour, 2016).

Boisseau R.P., Vogel D., and Dussutour A. (2016). Habituation in non-neural organisms: evidence from slime moulds. *Proceedings of the Royal Society B: Biological Sciences, 283,* 1829.

Dussutour A. et al. (2010). Amoeboid organism solves complex nutritional challenges. *Proceedings of the National Academy of Sciences, 107***,** 4607-4611.

Dussutour A. and Simpson, S.J. (2009). Communal Nutrition in Ants. *Current Biology, 19***,** 740-744.

Jeanson R., Dussutour A., and Fourcassié V. (2012). Key Factors for the Emergence of Collective Decision in Invertebrates. *Frontiers in Neuroscience, 6,* 121.

Vogel D. and Dussutour A. (2016). Direct transfer of learned behaviour via cell fusion in non-neural organisms. *Proceedings of the Royal Society London B., 283*(1845), 20162382.

Peter GODFREY-SMITH

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Minimal Cognition, Proto-Subjectivity, and Other Perplexities

I'll discuss some different ways of thinking about 'ground floor' questions in this area. These will include: the relation between living activity and cognition, the relation between simple forms of cognition and subjectivity, the relation between subjectivity and agency, and the possibility of strongly gradualist views on several questions about origins.

Biographical note:

Peter Godfrey-Smith is a philosopher of science, biology and cognition. His *environmental complexity thesis*—which holds that cognition functions to help an organism cope with environmental heterogeneity and dynamism (1996; 2002)—is central to this workshop, as is his concept of the *continuity thesis*, which raises the question of the degree to which life and cognition are co-extensive. He has written extensively on Darwinian selection, the evolution of altruism, the philosophy of biology, sender-receiver systems, biological information, and individuality. Most recently his interests turned to the cognitive powers (and possible subjective experience) of cephalopods (*Other Minds*, 2017) and the evolution of early nervous systems (Godfrey-Smith 2016; 2017).

Godfrey-Smith P. (1996). *Complexity and the function of mind in nature.* Cambridge: Cambridge University Press.

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

Godfrey-Smith P. (2013). Cephalopods and the evolution of the mind. *Pacific Conservation Biology*, *19*(1), 4-9.

Godfrey-Smith P. (2016). Mind, matter, and metabolism. *The Journal of Philosophy*, *113*(10), 481-506.

Godfrey-Smith P. (2017). *Other minds: The octopus and the evolution of intelligent life*. London: William Collins.

Pawel BURKHARDT

University of Norway

Origin and Evolution of Synaptic Proteins

How the first synapses and neurons evolved is an enigmatic subject that inspires much debate. Interestingly, key molecular building blocks of synapses and neurons are present in nerveless animals like sponges or placozoans. In addition, and even more surprising, many synaptic proteins are present in the closest unicellular relatives of animals. For example, we find that the choanoflagellates *M. brevicollis* and *S. rosetta* possess proteins that in animals spur neural precursor cells to develop into neurons. Moreover, a variety of pre- and postsynaptic-like proteins in choanoflagellates are present and some of them are transcriptionally co-regulated.

Here, I will present our recent discoveries on synaptic protein homologs found in choanoflagellates and explain how these fascinating protists help us to understand the evolutionary origin of synapses and neurons. First, we have biochemically and structurally characterized several presynaptic protein homolog complexes from choanoflagellates and gained insights into their molecular mechanism. Second, studies on post-synaptic scaffolding proteins reveal novel and conserved binding partners and hint towards the presence of a postsynaptic-like scaffold in choanoflagellates. Third, a recent understanding of how the enzyme CaMKII (CaMKII has an important role in long-term memory formation at animal synapses) functions at a molecular level emerged from studies on a CaMKII homolog from choanoflagellates. Fourth, we have used serial section transmission electron microscopy through choanoflagellate cells and sponge choanocytes to reconstruct regions with high abundance of secretory vesicles and identified different secretory vesicle types, but also observed unexpected differences between these two cell types. Our work highlights the need to include the closest unicellular relatives of animals to better understand the evolutionary origin of synapses and neurons and allows for a detailed understanding of when and how the first pre- and postsynaptic signalling machineries evolved.

Biographical note:

Pawel Burkhardt is a biologist whose research focuses on the evolutionary origin of synaptic proteins through studies of *choanoflagellates*, unicellular eukaryotes that are the closest living relatives of animals; *sponges*, animals with no synapses and neurons; and *ctenophores*, cilia-propelled neuralia also knowns as comb jellies (e.g. Sebé-Pedrós et al., 2013). He and his research group aim to understand the evolutionary history of the proteins required for synaptic activity, how they function at a molecular level, and which combinations of synaptic proteins resulted in the *origin of the neural synapse* (Burkhardt et al., 2011; Burkhardt et al., 2014; Burkhardt, 2015; Burkhardt & Sprecher, 2017). His work straddles the range from unicellular eukaryotes to neuralia.

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Frantisek BALUSKA

University of Bonn

Plant Cognition and Behavior

Current mainstream science considers plants passive organisms, not capable of cognition and behavior. This passive view of plants is due to their sessile nature. However, already in 1880 Charles and Francis Darwin had noted that this was an over-simplification. Moreover, evidence is emerging that plants actively sense their environment, use memory and learning in generating behavior, and implement plant-specific sensorimotor systems that are sensitive to anesthetics. Although plants are sessile, their organs move actively, and these movements are used to manipulate their environment, both abiotic and biotic. Moreover, the major strategy of flowering plants is to control animal pollinators and seed dispersers by providing them with food that not only is nutritious but also is enriched with manipulative and addictive compounds. Plants thus emerge as cognitive and intelligent organisms. There are even several examples of cognitive supremacy of plants over animals.

My ideas about plant cognition and behavior are based on cellular cognition, starting with archaea and bacteria, and are based on the synapse as a fundamental unit for generating complexity in information acquisition and transmission. Thus, cognitive principles enabled the evolution of higher levels of complexity in eukaryotic cells when host and guest cells negotiated their symbiosis (cells within cells). Likewise, the evolution of multicellular organisms involved a negotiation between eukaryotic cells that assembled into the tissues and organs of animals and plants. All cellular negotiation/communication happened at the synaptic domains. In this synaptic concept of biological evolution, intracellular synapses exist in eukaryotic cells; plant synapses organize plant tissues and organs; and epithelial synapses organize animal epithels. Neuronal-type synapses represent the most advanced synaptic organization that is fully devoted to processing sensory information and controlling organ movements.

Immuno-synapses enable negotiation of interactions between the cells of two organisms.

These synaptic/cognitive principles underlie biological organization, and have driven biological complexity to higher levels over the course of evolution. Plants not only evolved later than animals, they are more complex due to the inherent symbiosis between mycorrhizal fungi and plant roots, an ancient relationship that is also orchestrated by synapses.

Biographical note:

Frantisek Baluška is (mostly) a botanist interested in *plant signaling and behavior*, the long-time editor-in-chief of the journal of that name, and a pioneer in the study of *'plant neurobiology'*, which covers the many findings related to decision-making by root tips, signaling by action potentials, and other forms of intelligent information-processing in plants (e.g. Baluška, 2010; Baluška & Mancuso, 2013; Baluška et al., 2005). This work opens up new interpretations of what we might consider a 'nervous system' to be, making nervous systems more like other tissue forms (Baluška & Mancuso, 2009), as well as widening the notion of cognition (Baluška & Levin, 2016).

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Fred KEIJZER

University of Groningen

On the Origin of Subjects

Suppose one accepts current evidence that many or even most life forms exhibit various forms of intelligence: call it basal cognition. Would cognition as present in—at least some—animals be significantly different from that of other life forms? An affirmative answer faces at least two issues: (a) in what way would the difference be significant; and (b) why did this difference only occur within the animal lineage? One option is that though all life forms exhibit forms of information processing and signaling, the evolution of nervous systems vastly increased such information processing capabilities in animals. However, if an increase in information processing capacities is the single key factor, why have nervous systems not become much more common? Instead, I will articulate a proposal that addresses these issues by connecting the evolution of early nervous systems intrinsically to the origins of the animal sensorimotor organization or ASMO. The ASMO is posited as a multicellular unit capable of active contraction and extension, using feedback to track changes in its spatiotemporal form as well as external events that impinge upon any self-initiated changes. This organization constitutes an entity that can act as a basic subject, even a 'system of view', as it actively differentiates its own spatiotemporal self from an encompassing spatiotemporal world in which it acts. Such a basic subject provides an organization for additional sensory modalities to plug into as well as a scaffold where increasingly complex information processing can be put to adaptive use. Enabling such subject-based forms of cognition would count as being both significant and rare.

Biographical note:

Fred Keijzer is a psychologist-turned-philosopher with a main focus on *embodied cognition* and its implications for biological examples of intelligence. His early work challenged foundational assumptions of cognitivism, and pointed to the unappreciated complexity underlying the generation of ‘basic behavior’ in simple animals (Keijzer, 2001), including in bacteria (van Duijn et al., 2006). His current interests include the relevance of multicellular motility control for the evolution of *early nervous systems* (Keijzer et al., 2013) and how self-initiated motility may have provided a key role in the evolution of multicellular forms of sensing (Keijzer, 2015). He also works on a biological reconceptualization of cognition (Keijzer, 2017).

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Argyris ARNELLOS
University of the Basque Country

Individuality and Cognition: An Organizational Story of Co-Evolution

There is an apparent relation between the notions of (biological) individuality and cognition. We usually tend to ascribe cognitive capacities to adequately specified and demarcated biological entities. However, both concepts are theoretically blurred or (in a more well-disposed perspective) they come in different types. First, individuality can be of a metabolic/functional, evolutionary/Darwinian and/or organizational/organismal type. Second, as cognition is often seen as (any kind of a system's) adaptive interaction with the environment, cognition can be secretory/metabolic, motility-based, agent-based, etc. I will argue that, aside from some extreme positions, these different types (and features) of individuality and cognition can be tracked by an organizational approach. I will sketch various (relatively) early forms of different biological organization with a view to the possible co-evolution of individuality and cognition on the common basis of an organization's *integrative discontinuity* from the environment. For example, as individuality and cognition evolve there appears to be an increase in the functional integration among the various components and processes of the biological organization (the system becomes more and more integrated internally than it is externally integrated with its environment). At the same time, its motility- and action-based adaptive independence from the environment increases; the system becomes more and more capable to manipulate its environment. I will sketch the space of this co-evolution between organizational forms of biological complexity and types of cognition, and discuss several theoretical implications.

Biographical note:

Argyris Arnellos is a philosopher and theoretician who aims to specify clear, naturalistic and operationalized formulations and interpretations for various *concepts* and phenomena within the life sciences (Bich and Arnellos 2012;

Arnellos 2018). His focus is on the evolutionary changes constituting the transition to a multicellular organization. Examples are *multicellular individuality, autonomy and agency* (e.g., Arnellos et al. 2014; Arnellos and Moreno 2015, 2016). His work fits in with the *organizational (or autonomy) tradition* that moved away from classical autopoietic theory through various additions and refinements.

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Gáspár JEKELY

University of Exeter

Peptidergic Signaling at the Origin of Nervous Systems

Neuropeptides represent the largest class of neuronal signalling molecules in nervous systems. Over 30 families of neuropeptides and their specific G-protein coupled receptors were present in the last common ancestor of bilaterians. Neuropeptides are often involved in extra-synaptic volume transmission that can be largely independent of the synaptic connectivity of neurons. This together with the cell-type-specific expression of neuropeptides and their receptors suggests the possibility of a 'chemical wiring' of the nervous system that is distinct from its synaptic wiring. I will discuss examples of such chemical wiring and its implications for the origin of nervous systems. I will present our work on the systematic mapping of the neurosecretory centre in the larval apical organ of the marine annelid *Platynereis dumerilii*. I will also discuss our recent discovery of complex peptidergic signalling in the placozoan *Trichoplax adhaerens*, a millimeter-wide, flat, marine animal devoid of a nervous system and muscles. I will argue that peptidergic volume signalling may have predated synaptic signalling in the evolution of nervous systems.

Biographical note:

Gáspár Jékely is a developmental biologist working on the development and early evolution of nervous systems using *Platynereis* larvae (Jékely 2011), but who casts a wide net. Other research topics include the evolution of *phototaxis, vision systems (eyes),* the *connectome and circuitry* of both synaptic and paracrine signaling, and the self-organizing *cytoskeleton* in eukaryotes (Jékely 2013, 2014; Jékely et al. 2018). At the broader level of neural evolution he is interested in how nervous systems accommodate diverse constraints, such as dealing with external signals and internal coordination requirements as well as *integrating behavioral, developmental and physiological functions* (Jékely et al. 2015).

Jékely G. (2011). Origin and early evolution of neural circuits for the control of ciliary locomotion. *Proceedings of the Royal Society of London B: Biological Sciences*, *278*(1707), 914-922.

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Jékely G., Keijzer F.A., and Godfrey-Smith P. (2015) An option space for early neural evolution. *Philosophical Transactions of the Royal Society B*, 370, 201550181.

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Michael LEVIN

Tufts University

What Do Bodies Think About? Bioelectric Basis of Somatic Primitive Cognition in Embryogenesis, Regeneration, and Cancer

Embryogenesis reliably orchestrates individual cells towards a complex structural outcome. Regeneration repairs a correct anatomy from diverse injury states. How do cells make decisions about large-scale pattern? How do tissues know what to build and where, and when to stop growth and remodeling? To implement this remarkable plasticity, evolution capitalized on an ancient and ubiquitous system: bioelectrical signaling. Ion channels, present long before the appearance of specialized neurons, allowed cell networks to create electric circuits that implement pattern memory and distributed morphogenetic decision-making. The activity of bioelectric circuits implements a software layer between the genome and the anatomy. Our lab has developed novel techniques for reading and writing bioelectric states in vivo. I will introduce the mechanisms of developmental bioelectricity, showing how dynamics of distributed bioelectric circuits underlie large-scale morphological computation in embryogenesis, regeneration, and cancer suppression. I will also discuss our new computational and conceptual models of these processes as examples of cognition, exploiting learning and connectionist approaches to re-write the pattern memories that underlie control of growth and form. I will conclude with data showing an example of using these principles to create a novel life form that exhibits aspects of primitive cognition. These approaches link primitive cognition to new areas of evolutionary biology, regenerative medicine, and synthetic bioengineering.

Biographical note:

Mike Levin is a developmental biologist using molecular biophysics and computational modeling to probe the *information-processing mechanisms* that allow cells to *build and repair complex anatomies* (pattern homeostasis). Using organisms like planarian flatworms, frog embryos, and human organoids**,** the Levin lab works in *regeneration, embryogenesis, and synthetic morphology*. Specifically, they characterize bioelectric and neurotransmitter signaling mechanisms that coordinate the activity of somatic cells toward creation and remodeling of complex forms (Levin et al. 2017; Levin 2014a, 2014b). Their work has *identified ancient, proto-cognitive pathways* by means of which body tissues store pattern memories. The Levin lab has developed techniques to decode and re-write patterning goal states in vivo, enabling the rational control of growth and form using conceptual approaches homologous to cognitive neuroscience (Friston et al. 2015; Baluška and Levin 2016).

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Friston K., Levin M., Sengupta B., and Pezzulo, G. (2015). Knowing one's place: a free-energy approach to pattern regulation. *Journal of the Royal Society Interface*, *12*(105), 20141383.

Levin M. (2014a). Endogenous bioelectrical networks store non-genetic patterning information during development and regeneration. *The Journal of Physiology,* 592**,** 2295-2305.

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Detlev ARENDT

European Molecular Biology Laboratory-Heidelberg

Origin and Evolution of Central Nervous Systems

How animals progressed from a simple nerve net, as observed in basal metazoans, to complex centralized nervous system remains an exciting question in animal evolution. To trace this process, we are working on several animal model systems including the sea anemone as outgroup, as well as the marine annelid *Platynereis dumerilii*, and the chordate amphioxus. This helps us to unravel ancestral features of the nervous system that existed in the last common ancestors that these animals share with the vertebrates: the cnidarian-bilaterian ancestor (CBA), the urbliaterian, and the chordate ancestor. These were part of the evolutionary lineage where nervous system centralization occurred.

One major prerequisite for the comparison of nervous systems between remote species is the molecular identification and comparison of the neuron types that compose neural circuits, and an estimate whether or not these are homologous. To achieve this, we have generated cellular resolution expression atlases for our model species that allow mapping of neuronal transcriptomes that we obtain from single-cell sequencing of randomly picked cells from whole dissociated specimens. Also, in a community effort, we have provided a new definition of cell types as evolutionary units, moving away from phenotypic classification schemes.

I will focus on the reconstruction of the urbilaterian nervous system and present hypotheses on the degree of centralization that it had reached. This will involve analysis and interpretation of comparative data on the trunk nerve cord, peripheral nervous system, and the ‘apical nervous system’ that existed in these animals. From this reconstruction, I will discuss general principles of nervous system centralization.

Biographical note:

Detlev Arendt is a developmental biologist working on the evolution of *cell differentiation* in animals (Arendt 2008) and the origin and evolution of *early nervous systems* (Arendt et al 2015, 2016b). Recent collaborative work led to an evolutionary definition of cell types, and the concept of a 'core regulatory complex' of transcription factors for identifying them (Arendt et al. 2016a). His research group is also investigating the possible ways in which body plan, feeding behavior and locomotion came together (Arendt et al. 2015)**,** as well as how the transition to neuron-based coordination and control may have taken place. Another recent hypothesis is that calcium signaling may have originated as a cellular *damage response* before being recruited for neural signaling (Brunet and Arendt 2015).

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Eva JABLONKA
Tel-Aviv University

From Cognition to Consciousness: The Learning Route

The relation of cognition to consciousness, to subjective experiencing, is fraught with problems. It is self-evident that cognition in a general sense that can be applied to artefacts such as computers, is not a sufficient condition for subjectivity, but is cognition in *living organisms* necessary for subjectivity? Drawing on the discussions of basal cognition in the workshop, I argue that in living organisms, cognition is a necessary condition for the emergence of the only form of consciousness that we know, that of animals. Furthermore, as Simona Ginsburg and I suggested, a particular form of cognition, manifest as unlimited (open-ended) associative learning (UAL), has been both necessary and sufficient when animal consciousness first emerged during the Cambrian era. The operation of UAL, we maintain, can therefore be used as a positive marker for the presence of consciousness in animals (though the absence of UAL cannot be used to infer a lack of consciousness in extant animals). The paper ends with a discussion of some of the implications of this suggestion.

Biographical note:

Eva Jablonka is a geneticist and philosopher of science whose work with longtime colleague Marion Lamb on *epigenetics and epigenetic inheritance* has helped to revolutionize evolutionary biology over the past 15 years. Their seminal work (Jablonka and Lamb 2004) posits ‘four dimensions’ of inheritance upon which evolution can act: genetic, epigenetic, behavioral and cultural/symbolic. This work was extended in a collection of essays on the once-taboo subject of Lamarckism (Gnissis and Jablonka 2011), and is part of the current movement for an ‘extended evolutionary synthesis’ (Laland et al. 2015). Eva has a new book with Simona Ginsburg, currently in press, on the evolutionary origin of consciousness—*The Evolution of the Sensitive Soul: Learning and the Origins of Consciousness* (MIT Press)—in which they advance the novel hypothesis that consciousness is grounded in associative learning and may have contributed to the Cambrian explosion (Ginsburg and Jablonka 2010).

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Gissis S.B. and Jablonka E. (2011). *Transformations of Lamarckism: from subtle fluids to molecular biology*. Vienna Series in Theoretical Biology. Cambridge, MA: MIT Press.

Jablonka E., and Lamb M.J. (2014). *Evolution in four dimensions: genetic, epigenetic, behavioral, and symbolic variation in the history of life*, revised edition. Cambridge, MA: MIT Press.

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