

Programme: Venice Summer School in Evo-Devo 2017

Title: Process Thinking for Evo-Devo

Mon, Sep 18th: Introduction, History & Philosophy

09:00 – 10:00 Johannes Jaeger: introduction & overview

It is the central aim of evo-devo to understand the dynamics of evolving developmental processes, across scales of time and space. Yet, rather surprisingly, we have few tools to think and talk about processes. Instead, we are inclined to accept static accounts for the origin of traits, such as lists of genes or diagrams of regulatory networks. Studying the composition and structure of networks is an essential first step. In this course, we will not see it as an aim in itself but only as a first step towards more satisfying dynamic causal explanations. The course will provide the historical and philosophical background to understand the roots and importance of process thinking for evo-devo. It will explain philosophical and mathematical concepts that are necessary to understand developmental and evolutionary dynamics. It will provide concrete examples, where these principles and methods have been applied to specific evolving developmental systems. It will then examine the deep but problematic connection between pattern and process in evolution. Finally, it will end with a vision of evolution that is open-ended and fundamentally unpredictable, which makes biology quite unlike physics. The first lecture of the course will introduce the general setting and raise a number of questions that will then be addressed and discussed during the remainder of the week.

10:30 – 12:30 Scott Gilbert: history of process thinking leading up to evo-devo

There are numerous varieties of process thinking. Two of the major varieties are those involving flows and those involving dialectics. Thinking about processes as flows has been especially strong in notions of metabolism, where the organism or cell retains its identity solely by changing its parts. We flow through life as life flows through us. Thomas Huxley was one of the important figures in emphasizing this view of process. Waddington's use of Whiteheadian process philosophy brought notions of processes into the heart of embryology during the mid-Twentieth century. A second view of process involves dialectical exchange. This has been extremely important in the history of embryology. The notions of reciprocal embryonic induction can be viewed as dialectics, as can the interactions between sperm and egg, host and symbiont, receptor and ligand, nucleus and cytoplasm. The formulation of co-dependent origination, wherein entities co-develop with partners, has a rich embryological heritage and a philosophical tradition extending as far back as Nagarjuna. Such exchanges are also critical in theories of niche construction, which are related to those of embryonic induction. These processes will become very important in the formulation of evolutionary developmental biology, which presents itself as the physical basis for evolutionary change.

14:00 – 16:00 James DiFrisco: ontology of individual processes & individuals

This talk will examine how to think about the category of processes in the context of evolutionary developmental biology. The following questions will be addressed: What are processes? How do they relate to biological concepts like organism, mechanism, network, and character? What are the empirical and heuristic motivations for adopting a process-centered view in evolutionary developmental biology? How are processes classified? Can developmental processes be homologous, analogous, and/or modular? How does "process thinking" relate to "network thinking" in developmental biology? What does "process thinking" do for evo-devo?

16:30 – dinner Poster Session (voluntary)

Tue, Sep 19th: Dynamical Systems Theory – Concepts

09:00 – 10:00 Johannes Jaeger: introduction to dynamical systems theory

The questions posed by a process philosophical approach to evo-devo can be studied mathematically using dynamical systems theory. This lecture will take the concepts introduced by DiFrisco and show how we can describe developmental mechanisms and their properties in a mathematically rigorous way. We will introduce some basic concepts, the most fundamental of which is that of “flow,” which underlies all kinds of dynamical systems. We will examine how flows can be represented by vector fields, and how they can be simulated and analyzed using differential equations and the tools of phase space analysis. It is the geometry of phase space—encoded in the phase portrait—that determines the behavioral repertoire of a process. Multi-stable attractors can give rise to switch-like behavior, limit cycle attractors to periodic oscillations, while strange attractors produce deterministic chaos. Such different classes of phase space features provide us with a vocabulary that directly addresses the dynamic nature of the process. This lecture will focus on a non-technical, graphical introduction to these concepts and their meaning.

10:15 – 11:15 Nick Monk: phase space analysis I: autonomous systems

While the previous lecture introduced the basic concepts of dynamical systems theory, this lecture will provide specific methods and tools to study the phase portrait of so-called autonomous dynamical systems. Autonomous systems have variables that represent the system’s changing state, and parameters, which represent quantities like gene regulatory links that do not change over time. These systems have phase portraits that remain time-invariant. The geometry of the phase portrait—steady states such as attractors, their basins, and they are arranged with regard to each other— can be analyzed using classical tools such as linear stability analysis. It allows us to characterize the nature and robustness of each steady state, as well as the curvature and magnitude of the flow around them. We will introduce a number of specific tools that enable a rigorous qualitative understanding of the dynamics even if the underlying system is complex and non-linear. We will then examine how the phase portrait changes as parameter values are altered (e.g. if a gene network evolves and genetic links become altered). Steady states are created and annihilated by bifurcations, which themselves can be classified according to their geometric properties. We will provide numerous examples that illustrate the abstract concepts described above in simple toy models, such as the toggle switch or other simple models of gene regulation and cell-to-cell signaling.

11:30 – 12:30 Berta Verd: phase space analysis II: non-autonomous systems

The previous lecture introduced the powerful toolkit available for the study of autonomous dynamical systems. Unfortunately, most biological systems exhibit parameter changes over time, due to external signals, or changing environmental inputs over time. Dynamical systems with time-variable parameter values are called non-autonomous. Few standard tools exist to allow you examine their behavior. This lecture will use a simple toy model, a non-autonomous toggle switch, to illustrate new methods for studying the shape of dynamic trajectories in non-autonomous systems. We introduce a new classification of non-autonomous dynamical behaviors—transitions, pursuits, and captures—and show how they can be applied to the study of regulatory dynamics. These methods will be used on the next day to characterize a data-driven model of a specific real-world evolving patterning process.

13:30 – 16:30 Journal Clubs

Wed, Sep 20th: Dynamical Systems Theory – Examples

09:00 – 10:00 Nick Monk: context-dependent dynamics – Notch signalling

This second day of lectures on dynamical systems theory will illustrate the use of tools introduced on the previous day by the discussion of specific examples. The first of these lectures will examine how regulatory networks within cells are influenced by co-ordinated external signals, and how we best deal with this sort of complication in the context of dynamical systems theory. It will use models of lateral inhibition by Notch signaling to illustrate how dynamical systems modeling can be used to gain specific insights into the properties of spatial patterning during development.

10:15 – 11:15 Berta Verd: evol/dev dynamics of the gap gene network

Our second extended example is the evolving gap gene system in dipterans, a subsystem of the segmentation gene cascade. I will present a data-driven quantitative model of this pattern-forming gene regulatory network, that operates in the syncytial spatial context of the early blastoderm embryo. Gap genes interpret externally provided input by maternal morphogen gradients in different ways in the anterior and the posterior of the embryo. Even though the resulting patterns are similar, anterior gap domains form through a static switch-like mechanism, while shifting posterior domains are generated by a damped oscillator imposing temporal order on gap gene expression. This lecture will illustrate how the tools of non-autonomous system analysis can be used to understand and characterize the pattern-forming dynamics of the system. It will also discuss how the structure of the system alters the potential and dynamics of gap gene evolution, and illuminates the relative ease with which short- and long-germband insects can transition between fundamentally different modes of patterning.

11:30 – 12:30 Johannes Jaeger: of teeth, worms & limbs – other evo-devo models

This lecture will wrap up a day of examples with models that study the evolution of mammalian teeth, the vulva of roundworms, and the fin-to-limb transition in the evolution of land-dwelling tetrapods. Each of these models illustrates a specific point not covered by the two previous examples: the complex interplay between gene regulatory patterning and tissue dynamics, combinatorial evolution of signaling pathways and the prediction of variational properties, and self-organizing aspects of pattern formation and how they influence the evolvability of a system. I will conclude the lecture with a brief overview over some limitations of dynamical systems modeling, which fails to address some of the problems raised by a truly processual view of the world. I will discuss some possibilities how to overcome these limitations.

13:30 – dinner Topical discussions in small groups

Thu, Sep 21st: Evolutionary Dynamics

09:00 – 10:30 Ronald Jenner: pattern vs. process in phylogenetics

When biology became historical with the discovery of evolution, a dynamic world replaced the static order of things. This confronted biologists with a formidable epistemological challenge that required a shift of focus. To understand and explain the systematic distribution of taxa and their characters as being the result of evolutionary processes, biologists had to shift their attention from the tips of their systematic diagrams to the gaps between them. The relationships between organisms codified in the natural system were no longer abstract or of uncertain ontological status. Instead, they represented lineages of ancestors that were undergoing the open-ended process of evolutionary change. But unfortunately this process is inaccessible to observation or experiment. How could this evolutionary

world of invisible entities and events be accessed? This lecture explores how biologists have sought, and continue to seek, access to this empirically impenetrable realm of historical process. We will look at how embryos, fossils and extant taxa have been used to sketch ancestral outlines to root phylogenetic processes, and we will explore the pervasive influence of, often unreliable, evolutionary intuitions on the reconstruction of phylogenetic processes. We will briefly look at how the epistemological role of ancestors in phylogenetics was emasculated by the advent of cladistics and the concomitant return to a pattern approach to phylogenetics, and how in contrast evolutionary process considerations are the beating heart of molecular phylogenetics. We will discover how and why some influential practitioners of evo-devo take slippery shortcuts from evolutionary pattern to phylogenetic process, and we will finish by outlining the inherent limitations of our ability to reconstruct the macroevolution of body plans.

11:00 – 12:30 Graham Budd: pattern and process in morphological evolution

Discourse around various foundational aspects to evo-devo—such as gene expression patterns, heterochrony, homology, the nature of the phyla and the meaning of the fossil record—often makes rather dubious moves between pattern and process (and vice versa!) in order to generate explanatory hypotheses. I will critically examine some of the validating assumptions behind these moves in an attempt to disentangle these two aspects (where possible and desirable). My aim is to persuade that process is not simply a more fine-grained view of pattern, even if the two have the most intimate relationship. Process in evo-devo is thus underdetermined by pattern, and some other explanatory aspects need to be introduced in order to create a complete evolutionary explanation.

It is possible to see organisms as being processes (rather than as simply running processes within them); the consideration of them as the products of evolution adds a further dimension to this revised vision. This introduction of time as a critical aspect of evolutionary explanation will be illustrated by reference to the microevolutionary patterns exhibited by the trilobite-like arthropod *Agnostus pisiformis*, and the many scaling problems this creates will be discussed.

13:30 – 15:30 Stuart Kauffman: the emergence & evolution of life beyond physics

The emergence and evolution of life is based on physics but is beyond physics. Evolution is an historical process arising from the non-ergodicity of the universe above the level of atoms. Most complex things will never exist. Human hearts exist. Prebiotic chemistry saw the evolution of many organic molecules in complex reaction networks, and the formation of low energy structures such as membranes. Theory and experiments suggest that from this, the spontaneous emergence of self-reproducing molecular systems could arise and evolve. Such “collectively autocatalytic systems” cyclically link non-equilibrium processes whose constrained release of energy constitutes “work” to construct the same constraints on those non-equilibrium processes. Cells yoke a set of non-equilibrium processes and constraints on the energy released as work to build their own constraints and reproduce.

Such systems are living, and can propagate their organization with heritable variations, so can be subject to natural selection. In this evolution, these proto-organisms emerge unprestatably, and afford novel niches enabling, not causing, further types of proto-organisms to emerge. With this, unprestatable new functions arise. The ever-changing phase space of evolution includes these functionalities. Since we cannot prestate these ever new functionalities, we can write no laws of motion for this evolution, which is therefore entailed by no laws at all, and thus not reducible to physics. Beyond entailing law, the evolving biosphere literally constructs itself and is the most complex system we know in the universe.

16:00 – 18:00 Closing Discussion (moderator: Johannes Jaeger)