FIRST BORDEAUX-SAN SEBASTIAN WORKSHOP ON PHILOSOPHY OF BIOLOGY

PROGRAM

THURSDAY OCTOBER 20	
14:00 - 14:15	**Opening**
Session 1 ***Chair: Kepa Ruiz-Mirazo***	
14:15 - 15.15	**Some reflections on the concept of Functional Integration** Alvaro Moreno *IAS-Universidad del País Vasco*
15:15 - 16:15	**The immune system and the unification of the organism** Thomas Pradeu *ImmunoConcEpT, CNRS, University of Bordeaux*
16:15 - 16:45	***Coffee break***
16:45 - 17:45	**Beyond 'defence': Implication of the immune system in physiological and deregulated repair** Marie-Elise Truchetet *University Hospital of Bordeaux*
20:00	***Dinner***

FRIDAY OCTOBER 21 ***Session 3*** ***Chair: Derek Skillings***	
10:00 - 11:00	**An Eco-Immunity Account of Holobiont Individuality** Lynn Chiu *ERC IDEM, ImmunoConcEpT, CNRS, University of Bordeaux* [in collaboration with Gerard Eberl, *Microenvironment and Immunity Laboratory, Institute Pasteur]*
11:00 - 11:30	***Coffee break***
11:30 - 12:30	**Epigenetic Variation in Population Studies** Martha Susana Esparza Soria Arantza Etxeberria *IAS-Universidad del País Vasco*
12:30 - 14:00	***Lunch***
Session 4 ***Chair: Jon Umerez***	
14:00 - 15: 00	**The tyranny of scales in physics and biology** Sara Green *University of Copenhagen* [in collaboration with Robert Batterman, *University of Pittsburgh*]
15.00 - 15: 30	***Coffee Break***
15.30 - 16:30	**Capturing Processes: The Interplay of Modelling Strategies and Conceptual Understanding in Developmental Biology** Laura Nuño de la Rosa *IAS-Universidad del País Vasco*
16: 30 - 17:00	**Closing remarks and proposals**

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Abstracts

An Eco-Immunity Account of Holobiont Individuality

Lynn Chiu[1] & Gerard Eberl[2]

[1]ERC IDEM, ImmunoConcEpT, CNRS, University of Bordeaux

[2]Microenvironment and Immunity Laboratory, Institute Pasteur

Many resist the idea that the holobiont, the macro-organism "host" and its symbiotic micro-organisms, is a bona fide biological individual. For a group of individuals to be an individual in its own right, it must satisfy stringent conditions. These conditions not only ensure that the level of functionality and reproduction is truly at the level of the collective, they also guarantee that the collective persists as a whole. One requirement for persistence at the level of the group is that individual parts must be functionally integrated in particular ways. Some argue, on this basis, that the holobiont is not an individual: special and rare cases aside, the holobiont microorganisms comprise an ever shifting association of interacting ecological communities. Despite the enormous impact and importance of their livelihoods on each other, the host and its thousands of microbial communities are not functionally integrated in ways that support the persistence of the holobiont individual.

We do not disagree with this conclusion, but take issue with the criteria for persistence. Many principles of functional integration are articulated in terms of causal-functional interrelations that are internal to the individual. Since the holobiont is not internally integrated in the right way, by these criteria, it is not a persisting individual. However, from an immunological perspective, when these criteria of internal integration are applied to just the macroorganism host— not the holobiont—the host is not a biological individual as well. The persistence of the host is not supported internally, but by the tightly regulated, and mostly antagonistic, immune interactions with the constantly present microorganisms.

Criteria that reject both the individuality of the holobiont and the host are too stringent: they are not satisfied by any macroorganism. We thus construct an alternative criterion of functional integration that does not limit integrative relations to the internal domain. Based on the Equilibrium Model of Immunity (Eberl 2016), we argue that the persistence of a biological individual through change can only be supported by the integration of the right type of internal responses to the presence of a balanced set of external stimuli. Both the internal and external are important for the persistence of the individual (the host): the immunological machinery of the host alone is not integrated enough to maintain host persistence. However, the individual and its external stimuli as a whole (the holobiont) does not itself persist through change: they do not have internal responses to further external conditions. Insofar as holobionts are a general and basic existence on earth, our criterion supports a notion of life that is fundamentally symbiotic. Holobionts might not be biological individuals, but biological individuals cannot persist without their microorganisms.

Epigenetic Variation in Population Studies

Martha Susana Esparza Soria and Arantza Etxeberria

IAS-Research, University of the Basque Country (EHU/UPV)

Epigenetics has usually been conceived from an organismic perspective of development and inheritance, which in principle is not suitable for population studies. In contrast with classical Mendelian genetics, for which variation is generated blindly, epigenetic variation appears to be directed, produced in relation to the environments in which organisms live, and directly influenced by the "needs" encountered to adapt to those environments. Nevertheless, recent works pursuing a population epigenetics approach based on epigenetic variation, as well as models aiming to determine the rate of variation of heritable "epialleles" open new

research lines appropriate to study the population dynamics of non-genetic inheritance. In this paper, the differences and similarities of genetic and epigenetic variation will be examined, in order to consider the relevance of the population approach for epigenetics and to assess the novelty of the approach of population epigenetics.

The tyranny of scales in physics and biology

Sara Green[1] & Robert Batterman[2]

[1]Department of Science Education -University of Copenhagen

[2]Department of Philosophy – University of Pittsburgh

A common reductionist assumption is that macro-scale behaviors can be described "bottom-up", if sufficient details about lower-scale processes are given. The idea that an "ideal" or "fundamental" physics would be sufficient to explain all macro-scale phenomena has been met with criticism from philosophers of biology. Specifically, scholars have pointed to the impossibility of deducing biological explanations from physical ones, and to the irreducible nature of distinctively biological processes such as gene regulation and evolution. This paper takes a step back in asking whether bottom-up modeling is feasible even when modeling simple physical systems across scales. By comparing examples of multi-scale modeling in physics and biology, we argue that the reductionist must confront the "tyranny of scales" problem. The problem refers to the common challenge that multiple mathematical models are required to account for the scale-dependency of physical and biological behaviors. Different mathematical models are suited for modeling processes at different scales, and these rely on different boundary conditions. The need for inherently multi-scale strategies also has implications for the relation between physics and biology. In contrast to the assumption that appeals to physics in biology support mereological reductionism, we argue that inputs from physical science approaches in biology often stress the importance of tissue-scale parameters and models. We illustrate this through an examination of the role of biomechanics in multi-scale modeling of morphogenesis in developmental biology. In such contexts, the relation between models at different scales and from different disciplines is neither reductive nor completely autonomous, but interdependent.

Some reflections on the concept of Functional Integration

Alvaro Moreno

IAS-Research, University of the Basque Country (EHU/UPV)

The understanding of biological individuality is one of the most difficult problems for both philosophers and biologists. One of the reasons is that biological individuals deploy interactions among them, establishing synchronic collective functional networks, which often change dramatically the former way of life of their constitutive parts. In fact, these collective entities show a rich variety of relations between their parts and the whole, and only in certain cases these collective entities become in turn new individualities. The aim of this talk is to explore which kind of functional relations explain the different forms of relations between parts and wholes, and, specially, how integrated individualities emerge. In order to do that, I will analyze tree different cases of emergence of individuality: 1. The origin of proto-organisms; 2. The origin of eukaryotic cells; and 3. The origin of multicellular (integrated) organisms.

Capturing Processes: The Interplay of Modelling Strategies and Conceptual Understanding in Developmental Biology

Laura Nuño de la Rosa

IAS-Research, University of the Basque Country (EHU/UPV)

While a processual view of biological entities might be said to be congenial to embryologists, the intractability and speed of developmental processes has classically led to an epistemological abandon of processes in favour of the advantages of discretising ontogenies in arrays of patterns. It is not until the 2000s that the digital embryos obtained from in vivo microscopy have started to replace developmental series as the reference representations of development. In my presentation I will look at how new microscopy, molecular, and computer technologies for reconstructing biological processes are contributing to a processual understanding of development. First, I investigate how time-lapse imaging has brought with it a radical dynamization, not only of the images, but also of the theories of development themselves. Next, I explore the role that imaging technologies have played in the return of organicism in developmental biology. Finally, I focus on how quantitative imaging contributes to the explanation of developmental processes.

The immune system and the unification of the organism

Thomas Pradeu

ImmunoConcEpT, CNRS, University of Bordeaux

Though philosophers of biology have tended to pay little attention to immunology, I argue that discussions over biological individuality should take into account the lessons given by this major and extremely active domain. Indeed, immunity plays a pivotal role in biological individuality, for two main reasons: first, the immune system exerts its influence on every part of the living thing; second, it constitutes a discrimination mechanism, determining what sticks together as constituents of the organism (tolerance), and what doesn't (rejection). Importantly, this action of the immune system is not equivalent to the old self-nonself theory, because the immune system constantly responds to endogenous constituents and, conversely, it tolerates many exogenous entities, most prominently members of the microbiota. In this talk, I will explore the exact role of the immune system in this aggregation process, by which entities that are different and have different origins are associated into a common unit. I will also confront this immunological approach to physiological individuation with other approaches often mentioned in philosophy of biology, particularly evolutionary ones.

Beyond 'defence': Implication of the immune system in physiological and deregulated repair

Marie-Elise Truchetet

University Hospital of Bordeaux

The immune system is generally defined as a system of defence, selected through evolution for its capacity to insure host protection, mainly against pathogens. Yet, in addition, it has recently been increasingly conceived as a system of repair, as it seems to play a major role in how the organism not only perceives damages but also responds to them by reconstructing bodily constituents. To better characterize repair and distinguish it from cognate processes such as regeneration, it is useful to distinguish three kinds of possible restoration at the tissue level: the restoration of tissue integrity (which includes wound closure), the complete or partial restoration of tissue function, and finally the restoration of tissue architecture. In cases of deregulated repair, one or several aspects of tissue restoration can be affected. For example, fibrosis can be described as the result of a form of "over-repair" or "over-healing". Though the involvement of the immune system in repair has long been documented, research done in the last five years has shown that the immune actors involved in repair and the interactions between them and with non-immune components were much richer than expected. In an attempt to fill in the gap of the immune system/repair relationship, in this presentation we will first examine the role played by the immune system in repair, and second its implication in pathological settings of deregulated repair such as fibrosis.