Hosted by Department of Philosophy, Logic and Scientific Method

Lakatos Award Lectures

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Hashtag for Twitter users: #LSELakatos
@lsepublicevents  lse.ac.uk/events
Why Philosophy in Science? Re-visiting immunology and biological individuality
Two problems

- What is an individual in the living world?
- How does philosophy of science relate to science?
Two problems; two dissatisfactions; two claims

<table>
<thead>
<tr>
<th>What is an individual in the living world?</th>
<th>Evolution tells us what a biological individual is</th>
<th>Immunology is indispensable to understand biological individuality</th>
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<tbody>
<tr>
<td>How does philosophy of science relate to science?</td>
<td>Philosophy of science is a discourse on science</td>
<td>Philosophy of science would benefit from an interventionist attitude towards science</td>
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Plan

1. The need for a more inclusive philosophy of biology
2. Immunity, a critical contributor to biological individuality
3. A philosophy of immunology aiming at a multilevel contribution
4. The virtues of philosophy in science
1. The need for a more inclusive philosophy of biology
Study on Biology & Philosophy

- => 30 years of B&P.
- 2 main observations:
  - Domination of one biological field, evolution
  - Insensitivity to biological transformations
PNAS (2003-2015)

- Agriculture: 1%
- Anthropology: 2%
- Applied Biological Sciences: 2%
- Biochemistry: 12%
- Biophysics & Computational Biology: 9%
- Cell Biology: 8%
- Biophysics & Computational Biology: 9%
- Microbiology: 7%
- Medical Sciences: 10%
- Immunology & Inflammation: 7%
- Genetics: 5%
- Evolution: 5%
- Developmental Biology: 3%
- Environmental Sciences: 2%
- Ecology: 3%

Pradeu (2017)
Conclusion of this study

- The representations of biological domains in PNAS and B&P from 2003 to 2015 are **extremely different**.
- **Evolution**: The “5-60% rule”.
- => A “provincial” philosophy of biology.
Biology has much more to offer to philosophers

- Philosophy of biology has focused mainly on evolution.
- Some other biological areas are just as scientifically and philosophically interesting.
- Much is presently going on in these areas.
- Immunology is clearly one of them.
Why philosophy of immunology?

- Philosophically fascinating
- Scientifically extremely dynamic
- Very molecular
- Very conceptual and theoretical
- Link between biology and medicine
Why philosophy of immunology?

- Grafts
- Cancer
- Autoimmune diseases
- Infectious diseases
- Interactions btw hosts and infectious agents (- evolution)
- Ecoimmunology (- ecology)
- Neuroimmunology
- Individuality: biological individuals as composite but unified entities
- Metaphysics of science (e.g., genidentity)

Philosophically fascinating
What is immunology?

- Often defined as study of **defence** against pathogens.
- But much wider: grafts, cancer. Also development, repair, etc.
- Defining and delineating immunology is crucial. Philosophers can help.
2. Immunity, a critical contributor to biological individuality
The problem of biological individuality: Unity and persistence
A major problem throughout the history of philosophy
The problem of biological individuality in philosophy of biology

- One of the most discussed topics in PoB.
- Mainly based on evolutionary approaches (BIs as Els).
The problem of biological individuality in philosophy of biology

- One of the most discussed topics in PoB.
- Mainly based on evolutionary approaches (BIs as Els).
- A pluralistic approach is needed. Not simply plurality, but a combination of approaches and fields.
- Within this combination, immunology can play a major role.
Biological individuality and the ‘self’ in immunology

- **“Individuality” in immunology** (Richet 1894, 1913; Loeb 1930, 1937; Medawar 1957; Burnet 1962; Hamburger 1978). (See Tauber 1994).

- **Self-nonself** (Burnet 1969).
  - Acceptance of self
  - Rejection of nonself

- **Problems with self-nonself**

- **Immune-based individuality without “self”?**

- **Towards the idea of “heterogeneous individuality”**

From the critique of the self-nonself theory to the construction of the discontinuity theory

On the definition of a criterion of immunogenicity
Thomas Pradeu** and Edgardo D. Carosella*
- The speed of change
- Co-production with immunologists

PERSPECTIVES

ESSAY
The speed of change: towards a discontinuity theory of immunity?
Thomas Pradeu, Sébastien Jaeger & Eric Vivier

IMMUNOLOGY
The discontinuity theory of immunity
Thomas Pradeu¹* and Eric Vivier²,3*

PNAS | November 21, 2006
NATURE REVIEWS | IMMUNOLOGY
OCTOBER 2013
SCIENCE IMMUNOLOGY | PERSPECTIVE
14 July 2016
Induction of an immune response according to the discontinuity theory

Figure 2 | The induction of an immune response according to the discontinuity theory. The discontinuity theory states that the key to the induction of an immune response is antigenic difference in a time-dependent context. a | If structurally different motifs suddenly appear (that is, there is a strong quantitative difference with respect to time), then a vigorous immune response occurs, possibly followed by the generation of memory cells. b | In the case of a motif that is initially unusual but persists over time, the effector immune response is rapidly extinguished. c | If immune receptors interact with motifs that change very progressively (that is, there is weak quantitative variation with respect to time), then the immune response is weak and the motifs become tolerated. d | Finally, if a structurally different motif appears in an intermittent way, then a very strong and long-lasting immune response occurs.
Induction of an immune response according to the discontinuity theory

Box 2 | A mathematical model of the discontinuity theory
The speed of change
Co-production with immunologists

Recognition of patterns
Recognition of the absence of a pattern
Recognition of tissue damage
Recognition of functional modifications

From the critique of the self-nonself theory to the construction of the discontinuity theory
Which conception of immunology-based biological individuality?
Every organism is a complex “microbial” ecosystem

- A complex ecosystem made of many biotic elements, belonging to different species, and even kingdoms.
- Huge numbers of resident microbes.
- Microbiota: bacteria, but also viruses and fungi.
- In the gut, but also all body’s interfaces.
- Some of these microbes play a functional, sometimes indispensable, role. (Digestion, development, metabolism, immunity).
- They are not rejected by the immune system.

Functional roles of microbiota and immunological tolerance: true across species
The continuous unification of a plurality of constituents

- Every organism is an ecosystem, but a **strongly unified ecosystem**.

- Role of **immune system in this unification of a plurality** (*E pluribus unum*): inclusion/exclusion. Not endogenicity.

- The immune system is not the sole individuating device in living things, but it is **one of the most powerful devices**:
  - Ubiquitous (true across species)
  - Systemic (A constant immune control over the whole body in any living thing)
  - Selective (inclusion/exclusion)

- **A much more precise definition of physiological individuality.**

- **A re-definition of what an immune system is and does.**
An immunological definition of the organism

An organism = A physiological individual = a functionally integrated whole, made up of heterogeneous constituents that are locally interconnected by strong biochemical interactions and controlled by systemic immune interactions.

Test case: *Botryllus schlosseri*
Fusion vs. rejection in *Botryllus schlosseri*  

Rinkevich (2005), Natural chimerism in colonial urochordates
Combining physiological and evolutionary individuality

Organisms or biological individuals? Combining physiological and evolutionary individuality

Thomas Pradeu
3. A philosophy of immunology aiming at a multilevel contribution
Levels of knowledge and interactions between them

- General philosophy
- Philosophy of science
- Philosophy of biology
- Conceptual and theoretical biology
- Experimental biology
- Therapeutic applications

- Possible “leaps” between levels
- No hierarchy
Ambition to contribute to all these levels (and their interactions)
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<table>
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<th>General philosophy</th>
<th>Interactionist individuality</th>
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<td>Philosophy of science</td>
<td>Interventionist philosophy of science</td>
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<td>Philosophy of biology</td>
<td>Indispensability of immunity to understanding BI</td>
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<tr>
<td>Conceptual and theoretical biology</td>
<td>Discontinuity theory of immunity</td>
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<td>Re-definition of immunity as construction and repair</td>
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<td>Experimental biology</td>
<td>Kinetics of IR</td>
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<td>IS in repair; IS in TME</td>
<td></td>
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<tr>
<td>Therapeutic applications</td>
<td>Modulation of IS in repair-associated disorders</td>
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<tr>
<td>Promotion of “ecosystemic” medicine</td>
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Contributions to experiments

- Difficult and rare.
- **Some examples** of what we currently investigate with my group in the lab:
  - Are the mechanisms of immune-mediated tissue repair involved in **immune-promoted tumorigenesis**?
  - How different cell types **interact** in immune-mediated tissue repair? What is the role of **timing** in the recruitment of different cell types (or switching) in repair?
  - What kind of **immune memory gd** T cells display?
  - How to define conceptually and molecularly **immune stress** as a stimulus of immune cells, particularly **gd** T cells?
Importance of publishing in scientific journals

- Du Pasquier L. & Pradeu T. (forthc.), How to define immune memory?, *Immunological Reviews*.
4. The virtues of philosophy in science
Philosophy of science has been dominated by analyses on science

- Philosophy of science as a *discourse about science*, often at a very general and abstract level (theories, models, causation, etc.)
- Descriptive or prescriptive.
- Most scientists do not know what philosophy of science is, and when they do most of the time they don’t find it useful.
- From philosophy “on” science to philosophy “in” science
Major aim and characteristics of Philosophy in science

- To **produce science**, and **to influence science**.
- **Evaluated** as scientific.
- = “**Interventionism**”.
- **3 key features** of philosophy in science:
  - i) intervention in science; ii) recognized by scientists themselves as (potentially) fruitful for science; iii) in the short term.
- **Means:**
  - **Embedment** in scientific labs.
  - Acquisition of **scientific knowledge**.
  - Construction of a **common culture** (and language).
  - **Co-production** of knowledge. Co-writing of papers in both science and philosophy journals.
- **Only one approach** within philosophy of science.
What kinds of interventions?

- **Concepts**
  - Conceptual clarification leading to novel scientific investigations.
  - Critique of scientific concepts.
  - Suggestion of new concepts that can orient or re-orient empirical research.

- **Theories, models**
  - Identification of problems or gaps in existing theories or models.
  - Suggestion of new theories.
  - Unification of existing theories.

- **Bridges**
  - Between scientific disciplines (e.g., oncology, ecology, and evolution).

- **Experiments**
  - Suggest (or do) novel experiments.
Typical “philosophy in science” questions

- What do you mean exactly by this concept? (e.g., “immune memory”)
- Are you aware that you will probably do different experiments depending on the meaning (of a given scientific concept) you consider?
- Is this concept scientifically fruitful, or is it more like blinkers? (E.g. “self-nonself” for immunity in prokaryotes).
- What is the (explicit or implicit) theoretical and conceptual framework in which you conduct your research?
- Are you sure you have tested alternative views?
- Are you sure there are no contradictions in your framework?
- Do you feel the need to define your object of study, and why? (E.g., “immunity”, “development”, etc.)
There is nothing new in “philosophy in science”!

- Old wine in a new bottle? Just a name?
- Some philosophers and scientists have defended views that seem similar (e.g., Chang, Rovelli, etc.)
- Two replies:
  - First, putting a name on a phenomenon can help delineate and define it, and act as an incentive.
  - Second: Not new, but important and rare.
- The category PinS is reminiscent of others.
  - “Philosophy of science in practice”
  - “Complementary HPS”
- Reply: some important differences.
Philosophy of science in practice

- Strong move in recent philosophy of science.
- Remains in most cases a description of science, not a contribution to science.
Complementary science (Hasok Chang)

- “Complementary science – History and Philosophy of Science as a continuation of science by other means”
- Complementary science: what scientists neglect. Philosophy in science: what some scientists see that they should not neglect.
- Corresponds to the “participatory” mode of Chang (1999).
- This is where the co-writing w/ scientists and publishing in scientific journals become important.
- An elitist approach to science? Yes, at least in part.
Philosophy of science & Philosophy in science

- Philosophy of science
- Philosophy in science
- Complementary science
- Science
Successes will be rare

- Aim: a recognized contribution to science, most of the time in collaboration with scientists and in a scientific journal.
- Contribution to science, philosophy of science, and philosophy.
- Very difficult. More failures than successes are to be expected.
- Worth trying.
An Institute for Philosophy in biology and medicine

[Image of the institute's logo]

Institute for Philosophy in Biology and Medicine
CNRS & University of Bordeaux, France

https://www.philinbiomed.org/

- **4 main guiding principles:**
  - Interventionism
  - "Embedded" philosophers
  - Co-writing of papers in both science and philosophy journals
  - Common reading groups

- **International network** of similar initiatives (Sydney, MBL, Cambridge, Exeter, etc.)
Conclusion

- Immunology is crucial to define biological individuality.
- Organisms can be understood as strongly unified ecosystems, under the control of an immune system.
- Philosophers can directly contribute to science, in collaboration with scientists.
- Philosophy in science, based on interventionism, should become a major approach in philosophy of science.
- A pivotal challenge will be the training of philosophers-scientists.
Acknowledgements

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- [https://www.immuconcept.org/conceptual-immunology/](https://www.immuconcept.org/conceptual-immunology/)