Hosted by Department of Philosophy, Logic and Scientific Method

Lakatos Award Lectures

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Dr Brian Epstein
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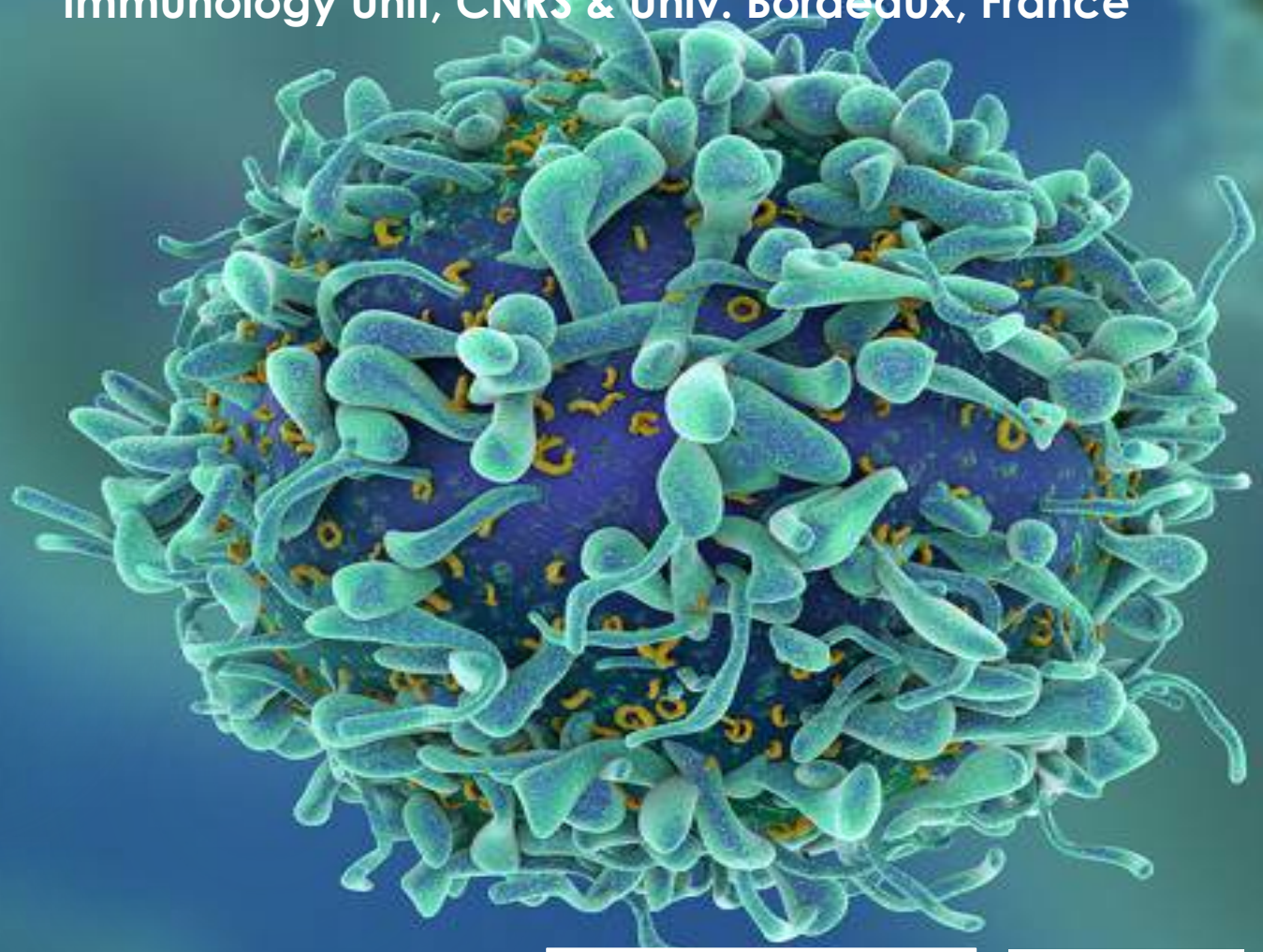
Lakatos Lecture, LSE
Nov 9, 2017



Why Philosophy in Science? Re-visiting immunology and biological individuality

ImmunoConcEpT
Immunologie conceptuelle expérimentale translationnelle

PhilInBioMed

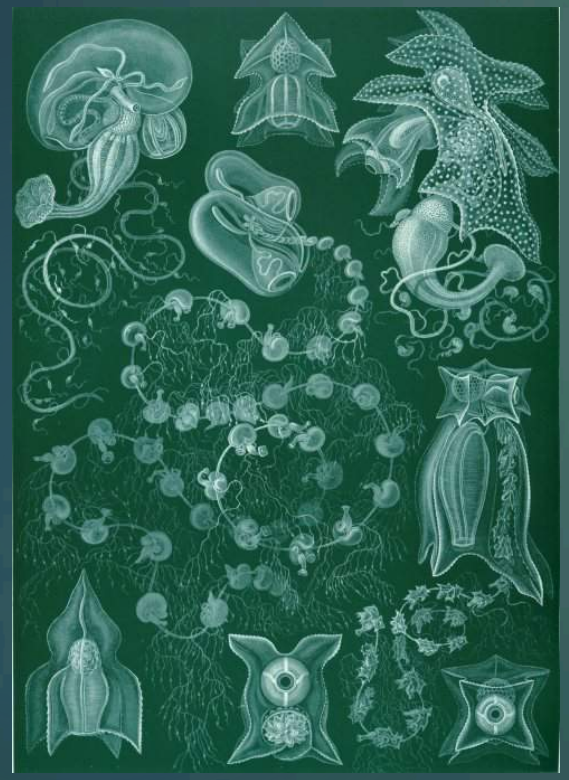
université de BORDEAUX

erc

cnrs
dépasser les frontières

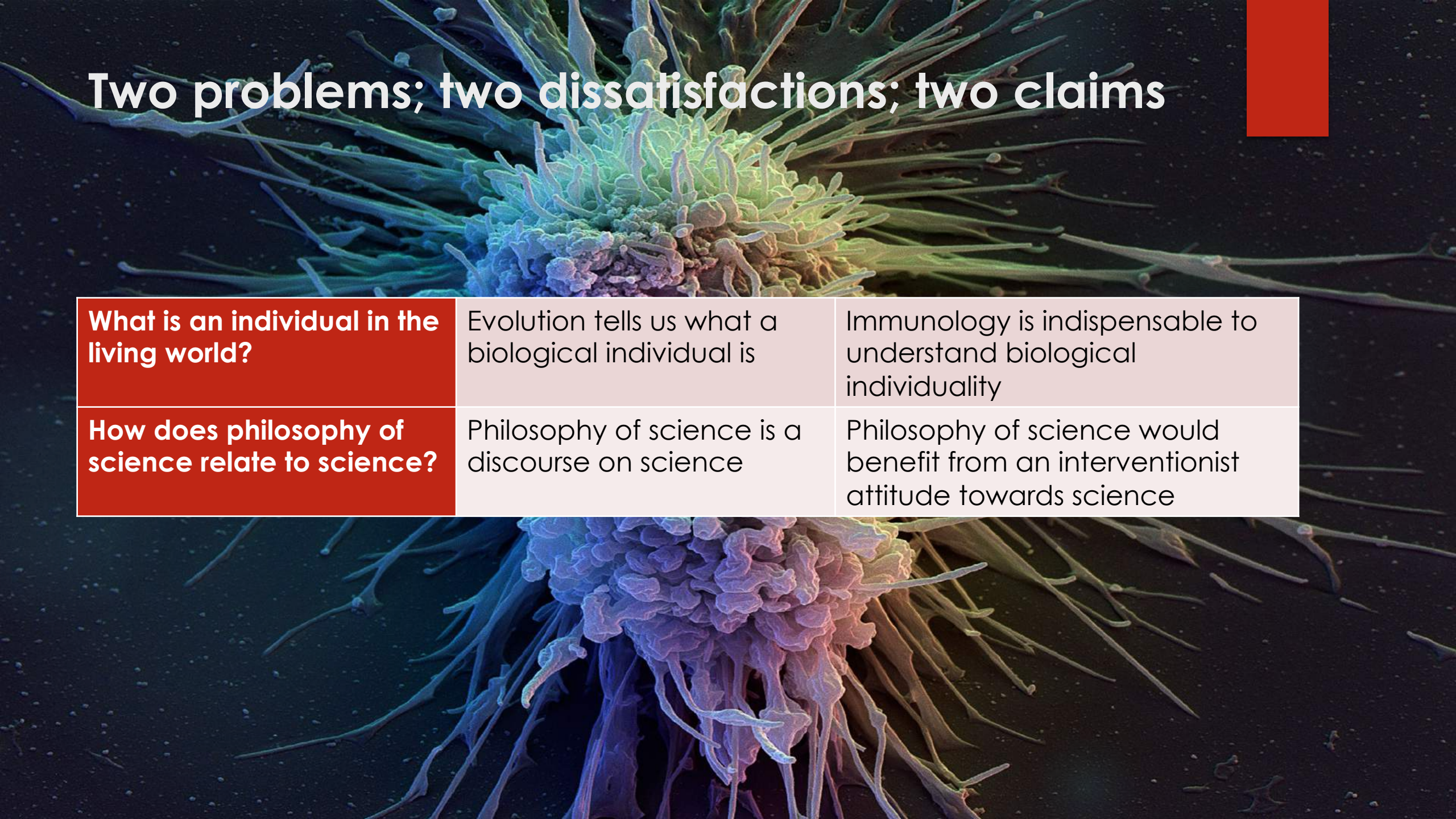
Two problems

- What is an individual in the living world?



- How does philosophy of science relate to science?

Two problems; two dissatisfactions; two claims



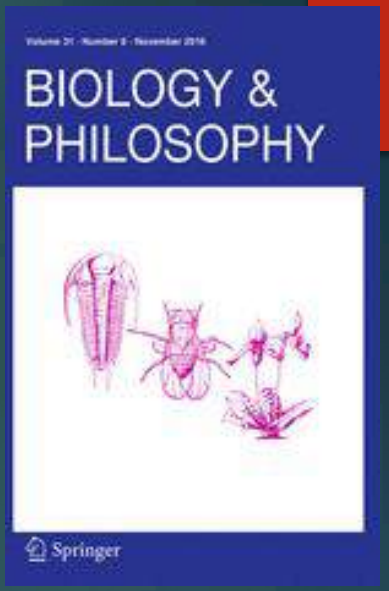
What is an individual in the living world?	Evolution tells us what a biological individual is	Immunology is indispensable to understand biological individuality
How does philosophy of science relate to science?	Philosophy of science is a discourse on science	Philosophy of science would benefit from an interventionist attitude towards science

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*



- Study by Gayon (2009) on 1986-2002.
- Study by Pradeu (2017) on 2002-2015.
- => 30 years of *B&P*.
- 2 main observations:
  - Domination of one biological field, evolution
  - Insensitivity to biological transformations

Philosophy of Biology: An Historico-Critical Characterization

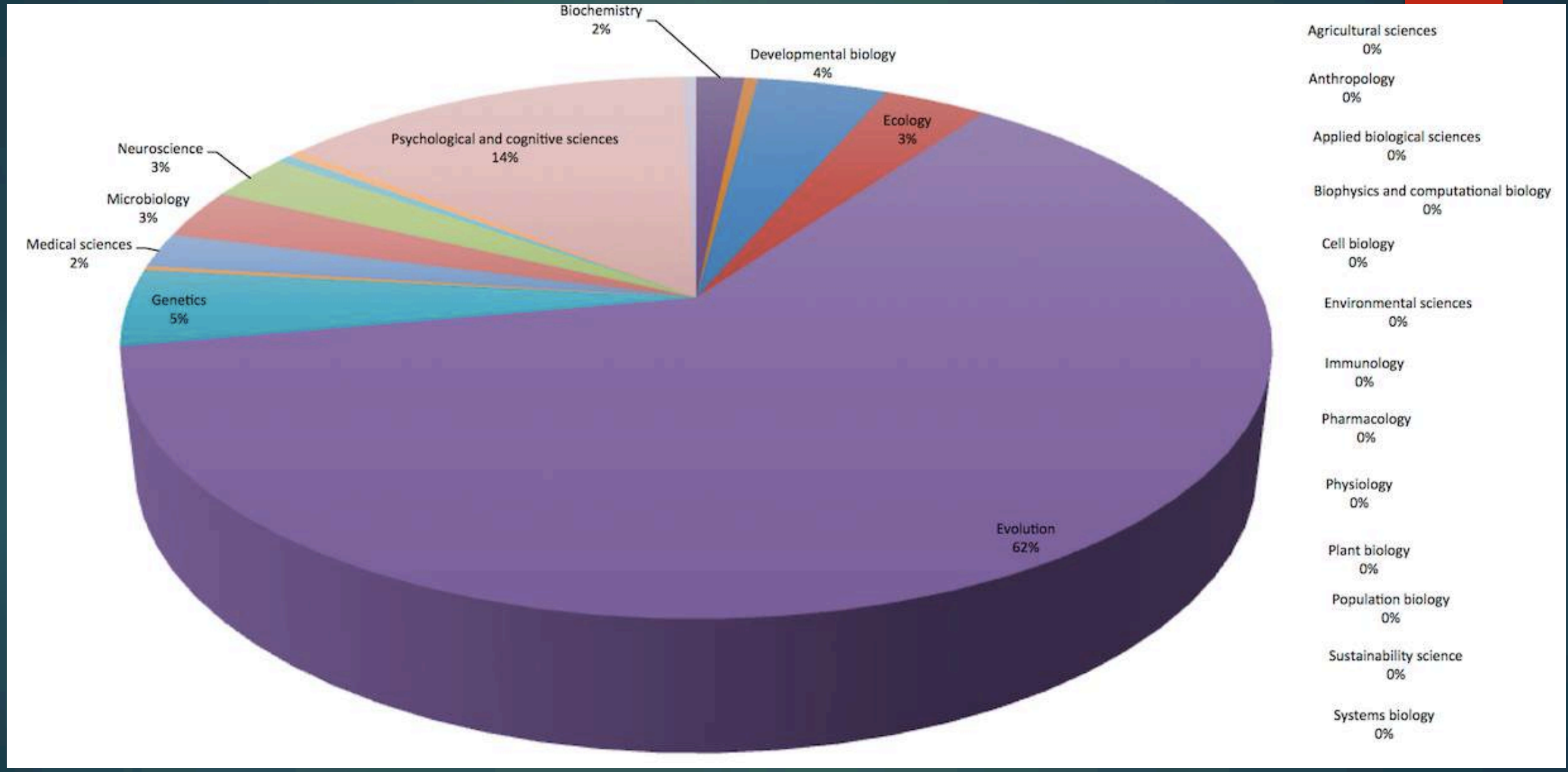
Jean Gayon

Biol Philos (2017) 32:149–167
DOI 10.1007/s10539-016-9558-7

Thirty years of *Biology & Philosophy:* philosophy of which biology?

Thomas Pradeu[1,2]

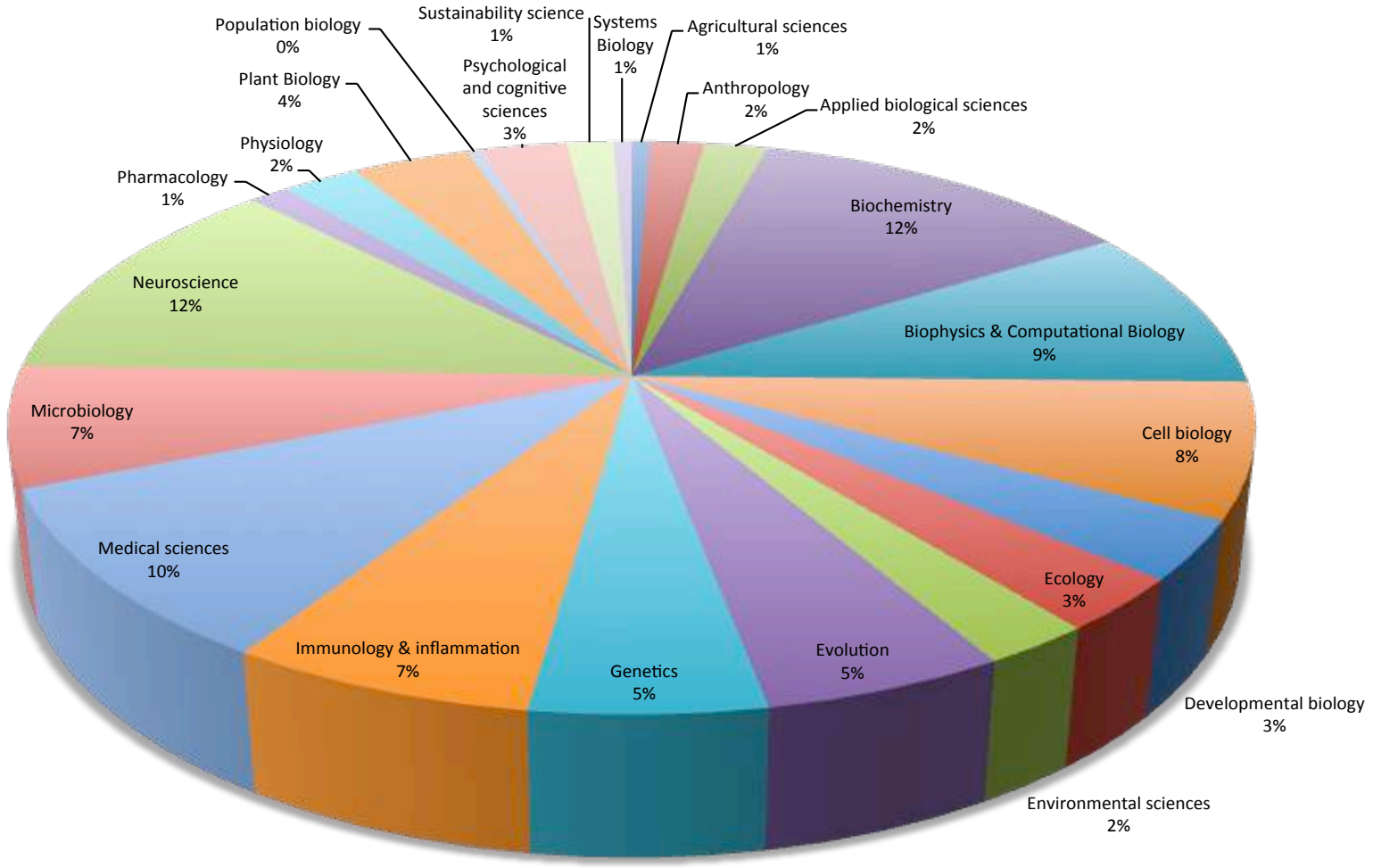
B&P (2003-2015)



- Pradeu (2017)

PNAS (2003-2015)

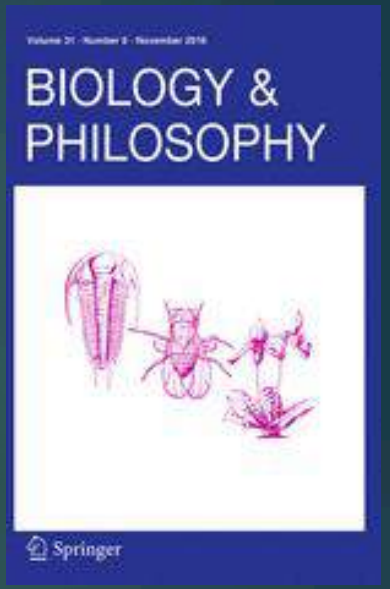
PNAS 2003-2015



- Pradeu (2017)

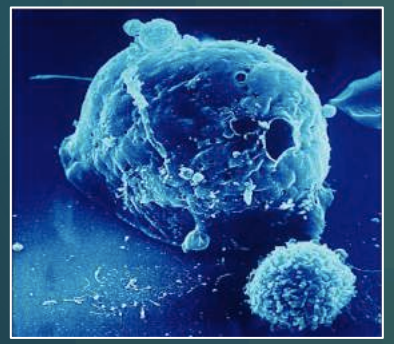
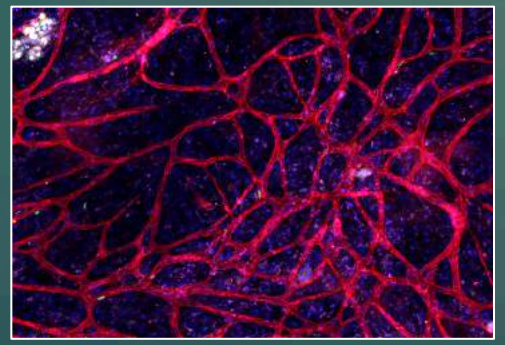
Conclusion of this study

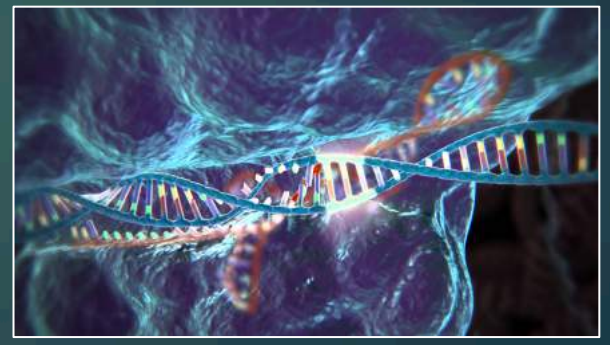
- The **representations** of biological domains in *PNAS* and *B&P* from 2003 to 2015 are **extremely different**.
- **Evolution**: The "5-60% rule".
- => A **"provincial" philosophy of biology**.



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.

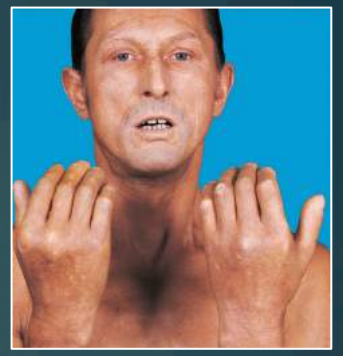



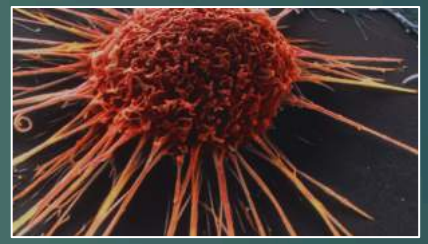


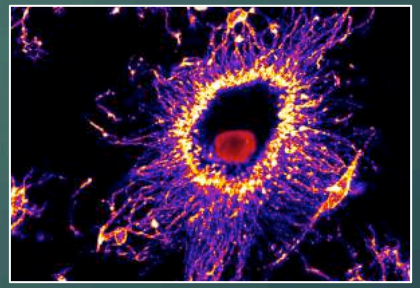
Why philosophy of immunology?

- Philosophically fascinating

- Scientifically extremely dynamic
- Very molecular
- Very conceptual and theoretical
- Link between biology and medicine



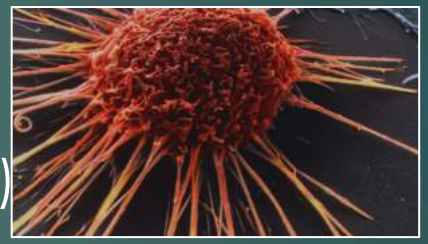


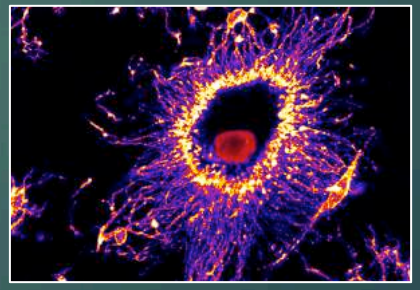


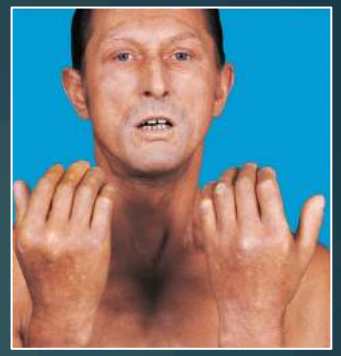
Why philosophy of immunology?

- Philosophically fascinating

- 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)





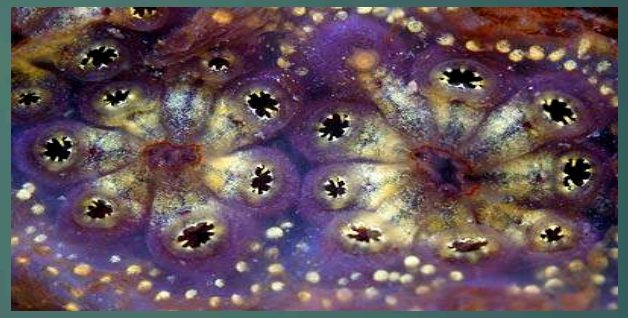


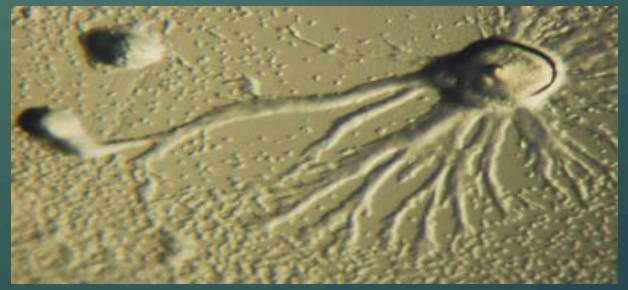
What is immunology?

- 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.

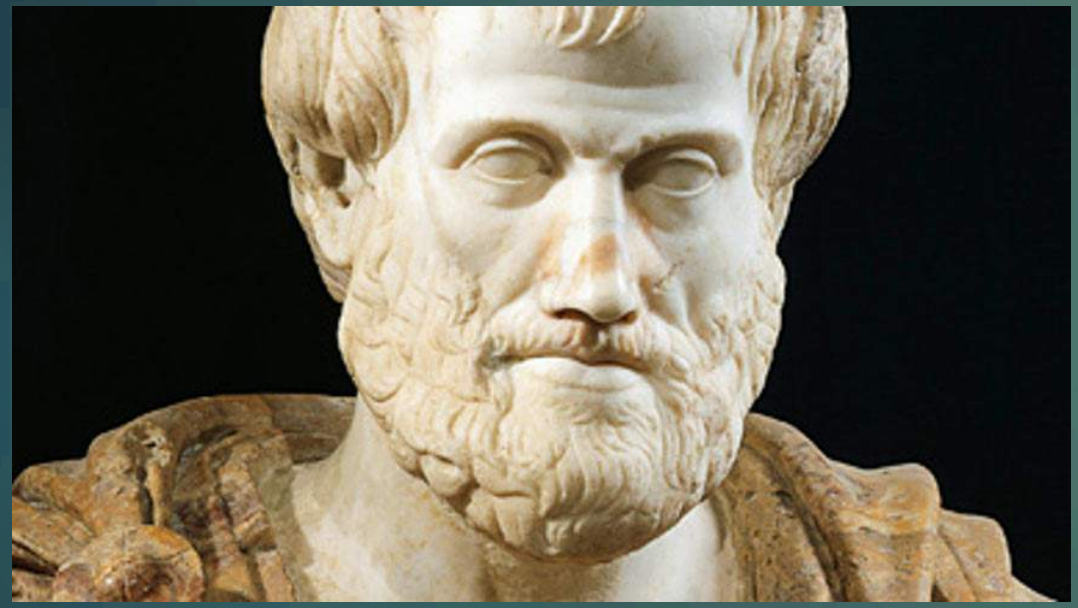
2. Immunity, a critical contributor to biological individuality

The problem of biological individuality: Unity and persistence



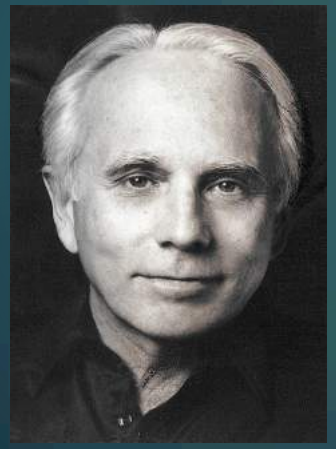


A major problem throughout the history of philosophy

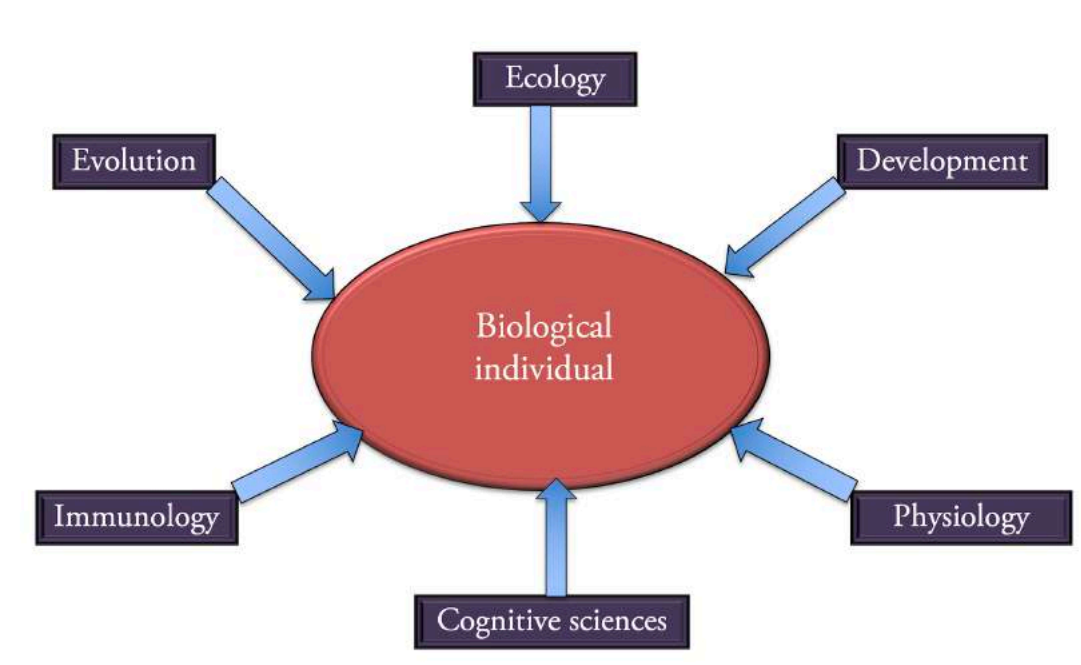


The problem of biological individuality in philosophy of biology

- One of the most discussed topics in PoB.
- Mainly based on **evolutionary** approaches (BIs as EIs).




The problem of biological individuality in philosophy of biology



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

Biol Philos (2016) 31:761–773
DOI 10.1007/s10539-016-9553-z

EDITORIAL

The many faces of biological individuality

Thomas Pradeu[1]

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"**

Pradeu, *The Limits of the Self: Immunology and Biological Identity*, 2012.

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‡

PNAS | November 21, 2006

- 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

NATURE REVIEWS | IMMUNOLOGY

OCTOBER 2013

IMMUNOLOGY

The discontinuity theory of immunity

Thomas Pradeu[1]* and Eric Vivier[2,3]*

SCIENCE IMMUNOLOGY | PERSPECTIVE

14 July 2016

Induction of an immune response according to the discontinuity theory

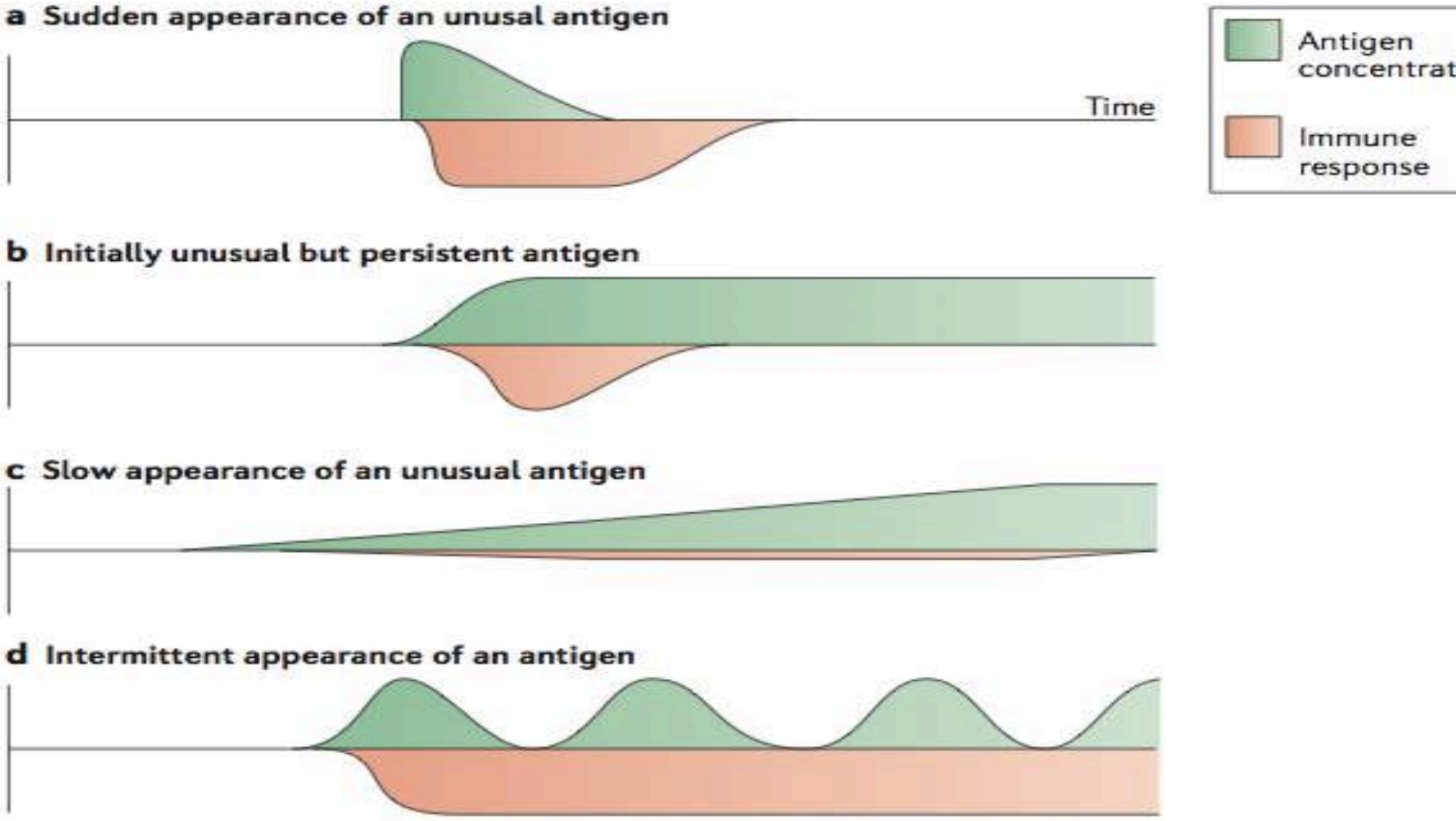


Figure 2 | **The induction of an immune response according to the discontinuity theory.** discontinuity theory states that the key to the induction of an immune response is antigenic di ence in a time-dependent context. **a** | If structurally different motifs suddenly appear (that is, th is a strong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

PERSPECTIVES

ESSAY

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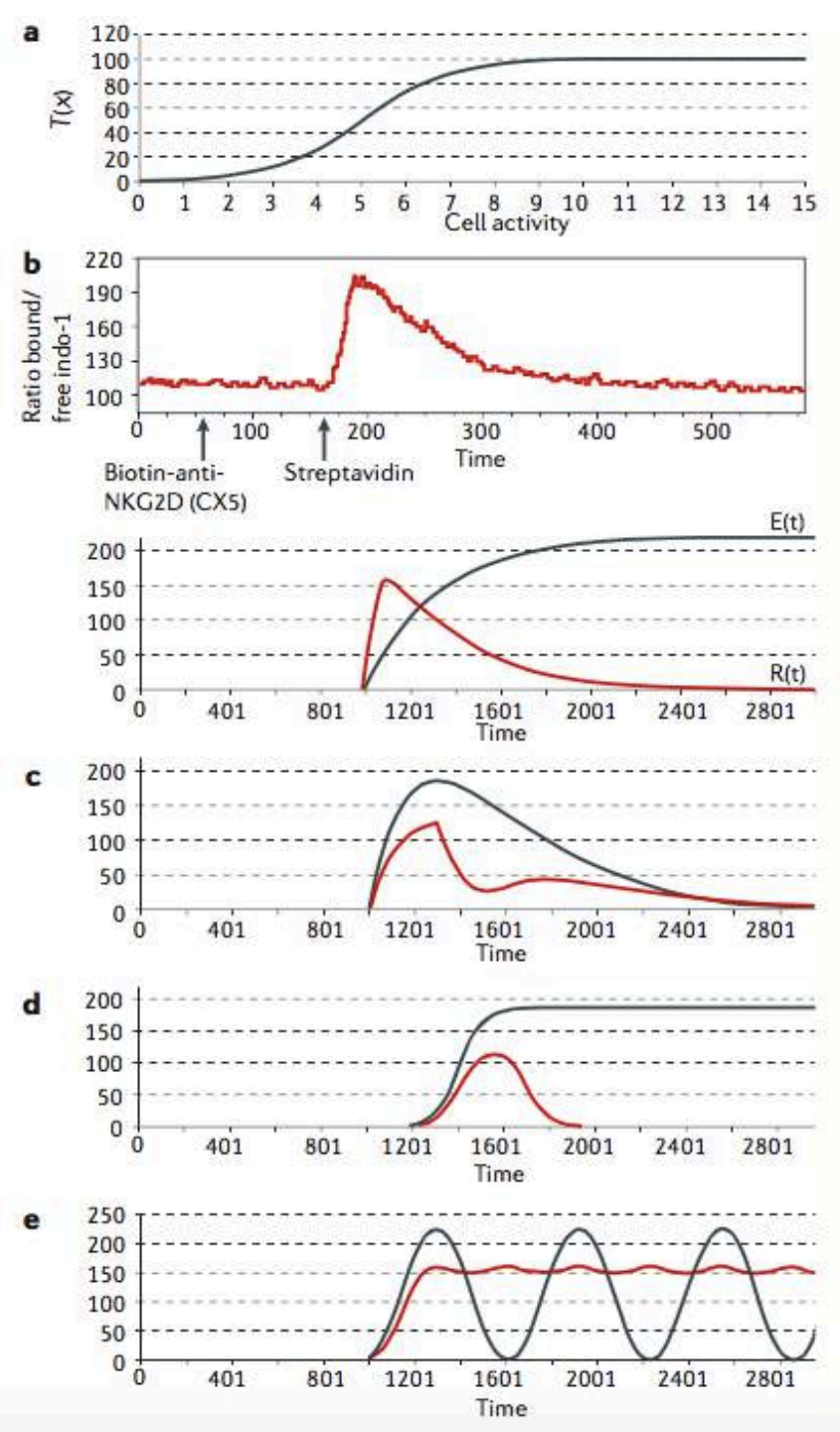
Thomas Pradeu, Sébastien Jaeger & Eric Vivier

Induction of an immune response according to the discontinuity theory

Box 2 | **A mathematical model of the discontinuity theory**



PERSPECTIVES

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- The speed of change
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PERSPECTIVES

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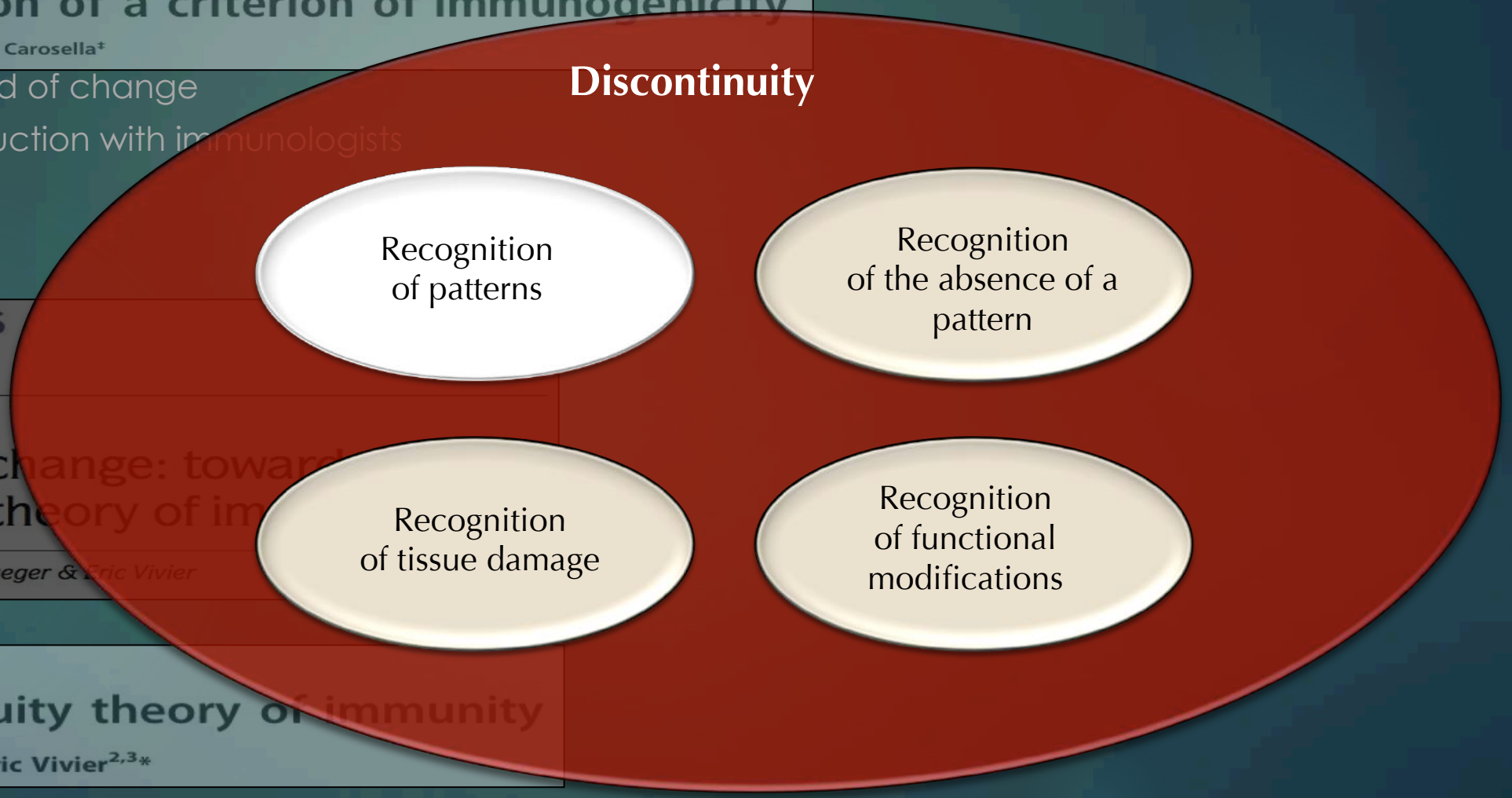
The speed of change: toward discontinuity theory of im

Thomas Pradeu, Sébastien Jaeger & Eric Vivier

IMMUNOLOGY

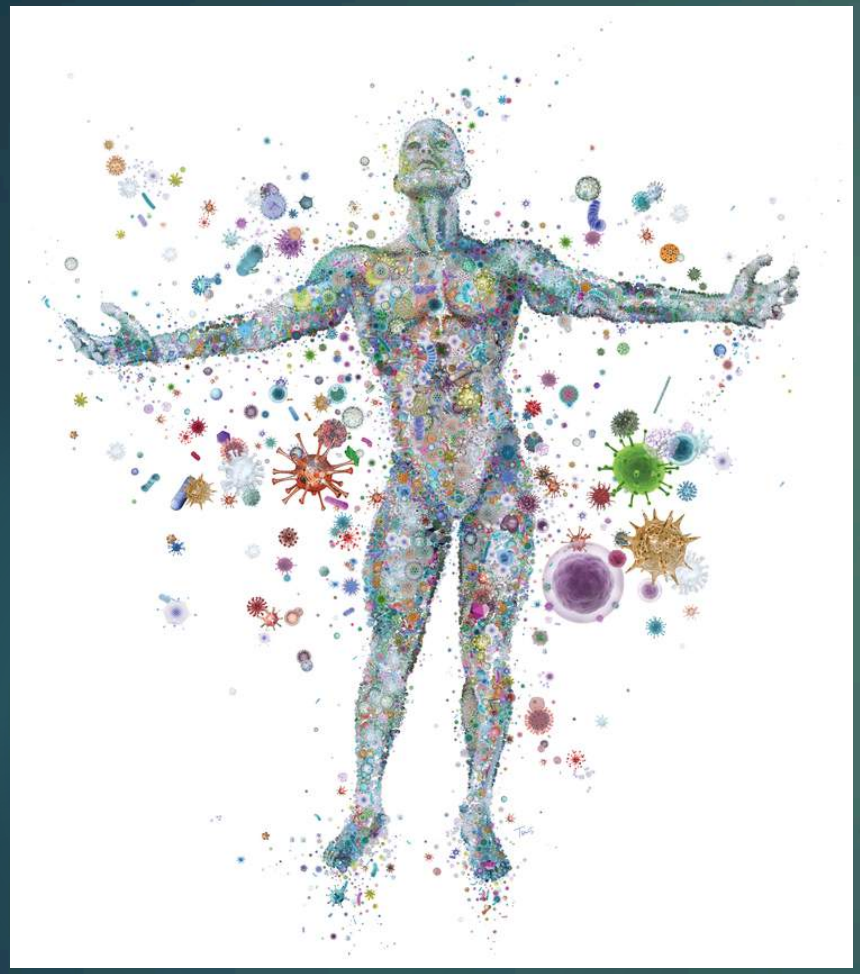
The discontinuity theory of immunity

Thomas Pradeu[1]* and Eric Vivier[2,3]*



- **Which conception of immunology-based biological individuality?**

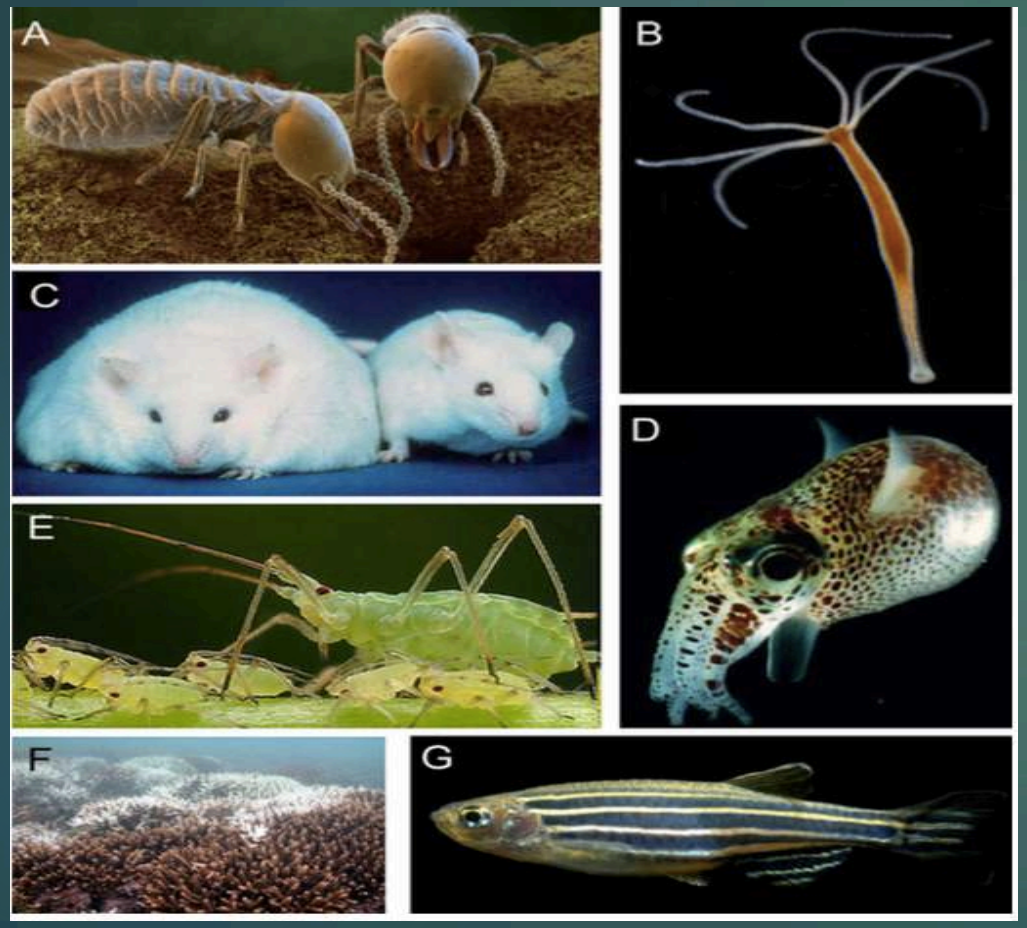
Every organism is a complex "microbial" ecosystem



- 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**.

Dethlefsen et al. (2007). An ecological and evolutionary perspective on human–microbe mutualism and disease. *Nature*.
Bosch, T. C., & McFall-Ngai, M. J. (2011). Metaorganisms as the new frontier. *Zoology*, 114(4), 185-190.

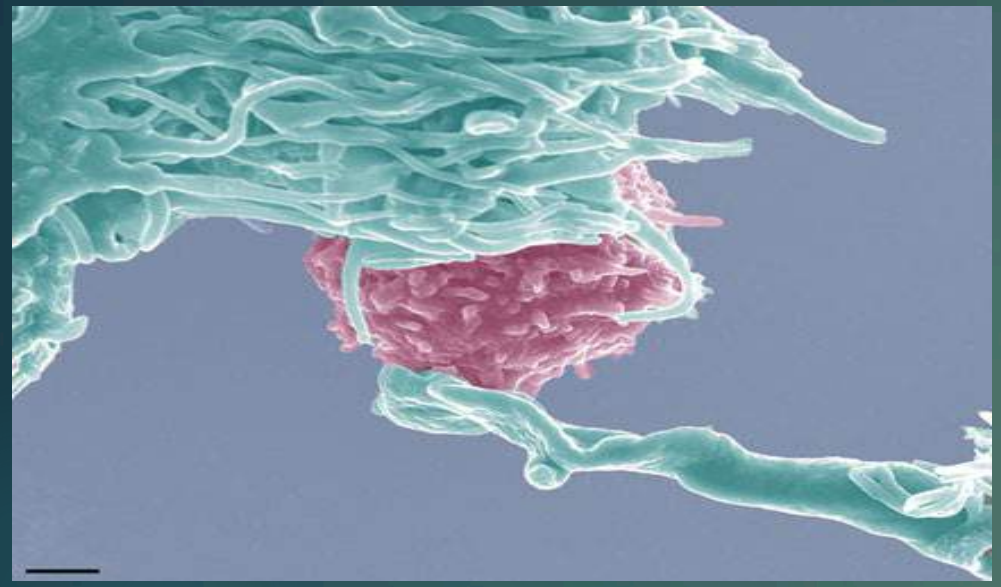
Functional roles of microbiota and immunological tolerance: true across species



Metaorganisms as the new frontier

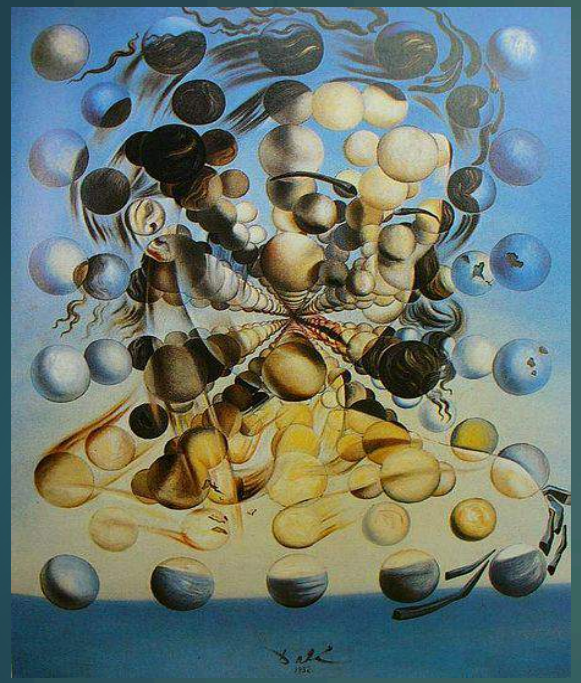
Thomas C.G. Bosch[a,*], Margaret J. McFall-Ngai[b]

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

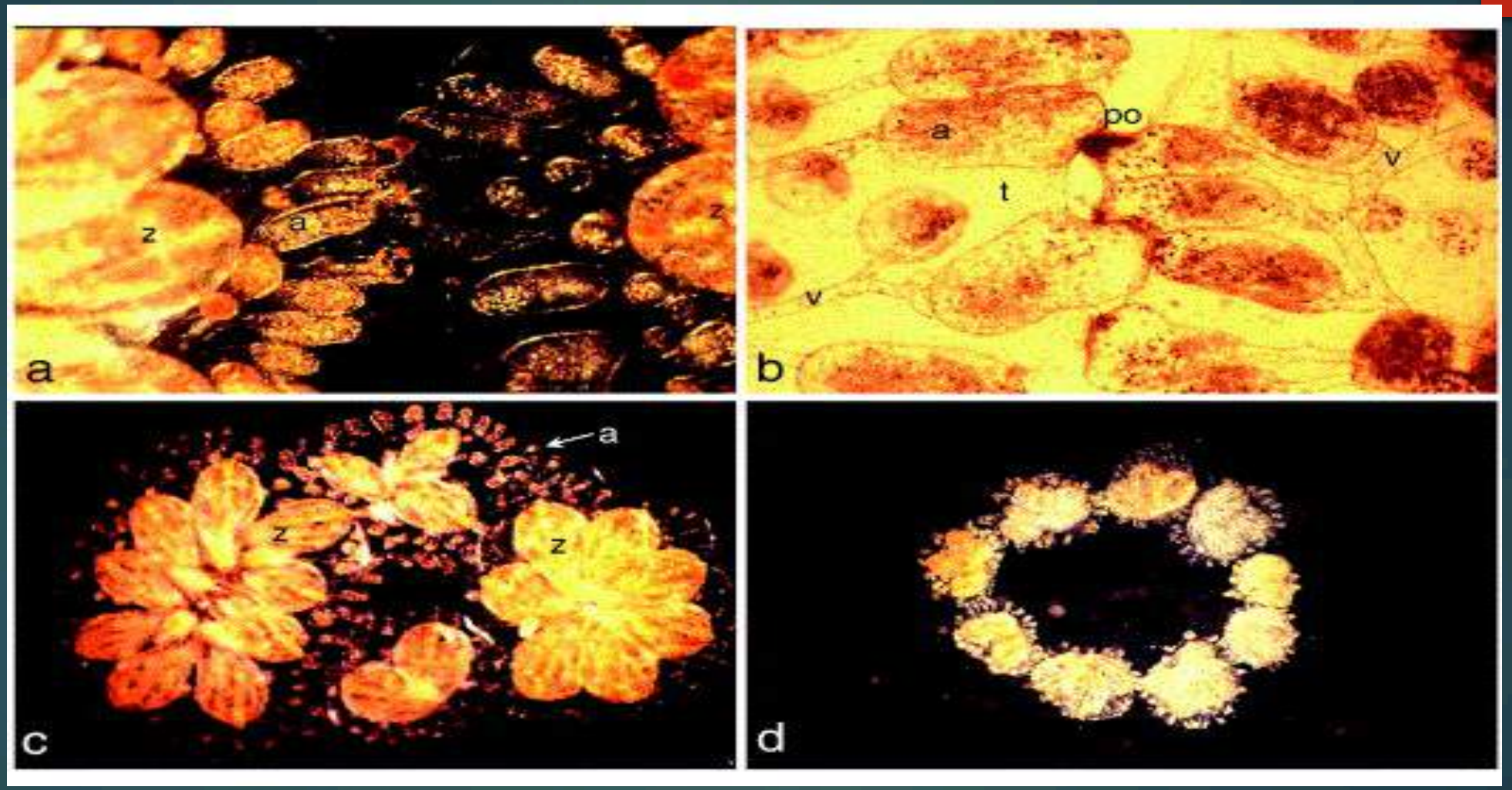


An organism = A *physiological* individual = *a functionally integrated whole, made up of heterogeneous constituents that are locally interconnected by strong biochemical interactions and controlled by systemic immune interactions.*

- Pradeu (2010), What is an organism? An immunological answer, Hist. Phil. Life Sci., 32 (2010), 247-268.

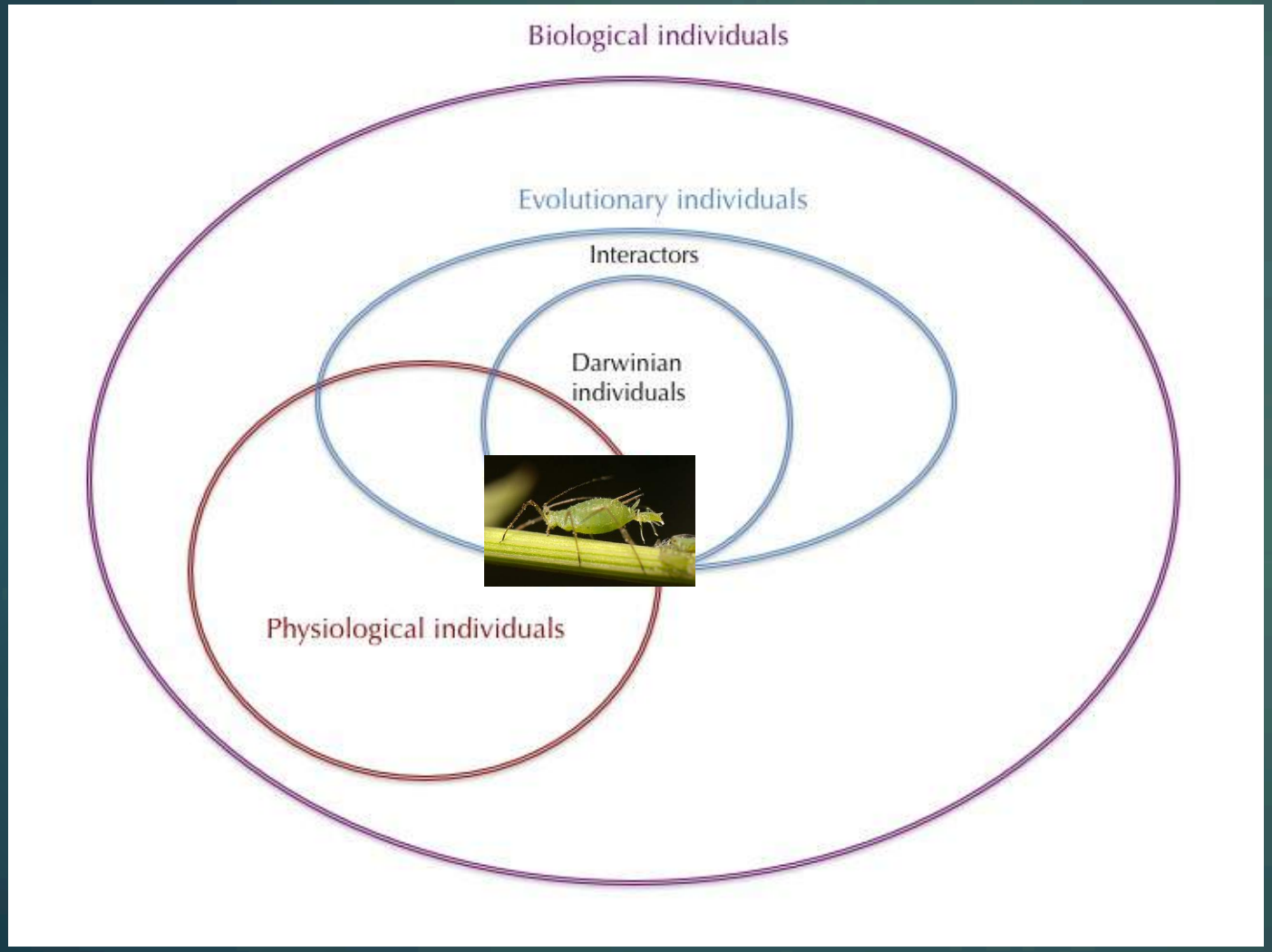
Test case: *Botryllus schlosseri*

Fusion vs. rejection in *Botryllus schlosseri*



Rinkevich (2005), Natural chimerism in colonial urochordates

Combining physiological and evolutionary individuality



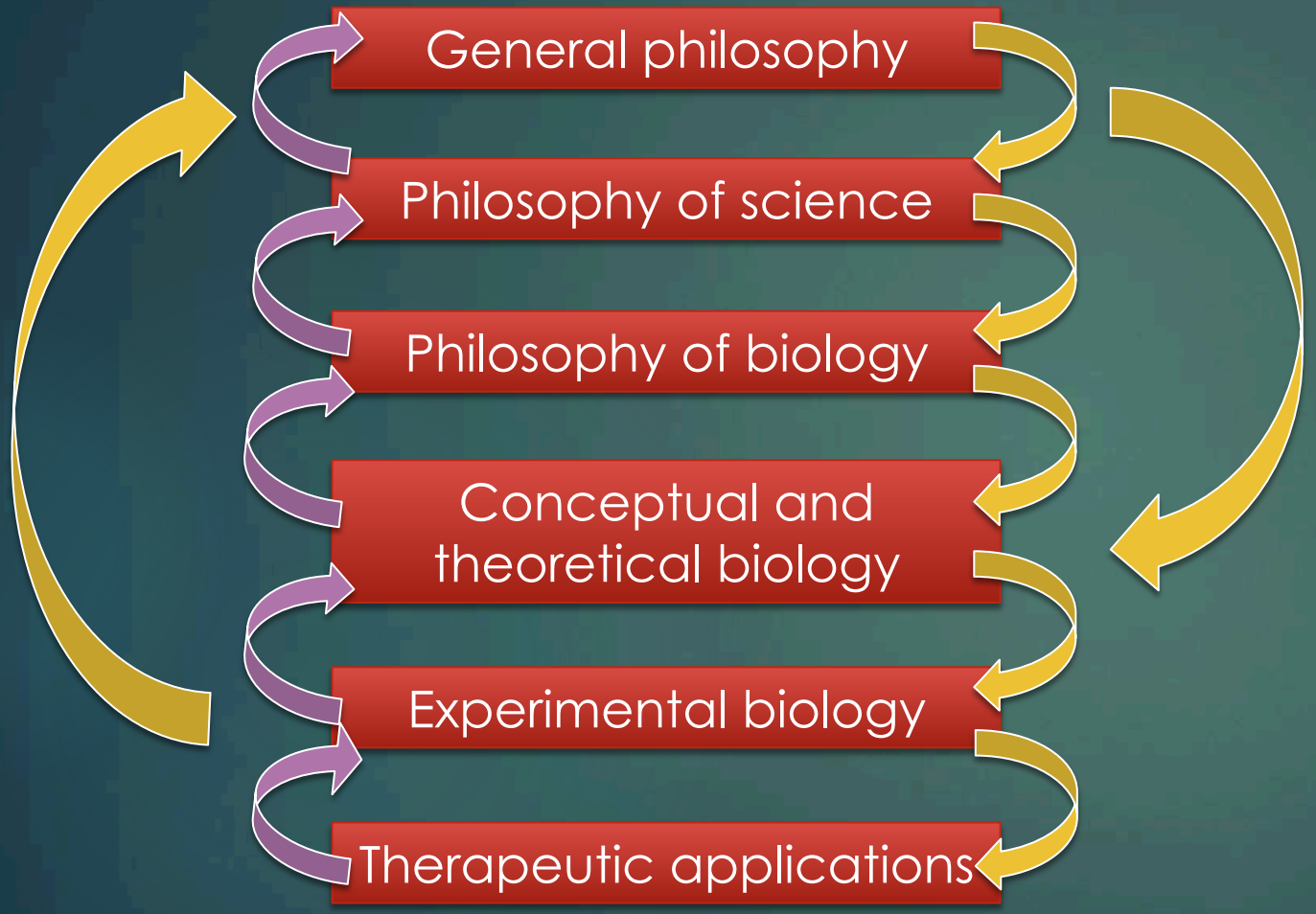
Biol Philos (2016) 31:797–817
DOI 10.1007/s10539-016-9551-1

Organisms or biological individuals? Combining physiological and evolutionary individuality

Thomas Pradeu[1]

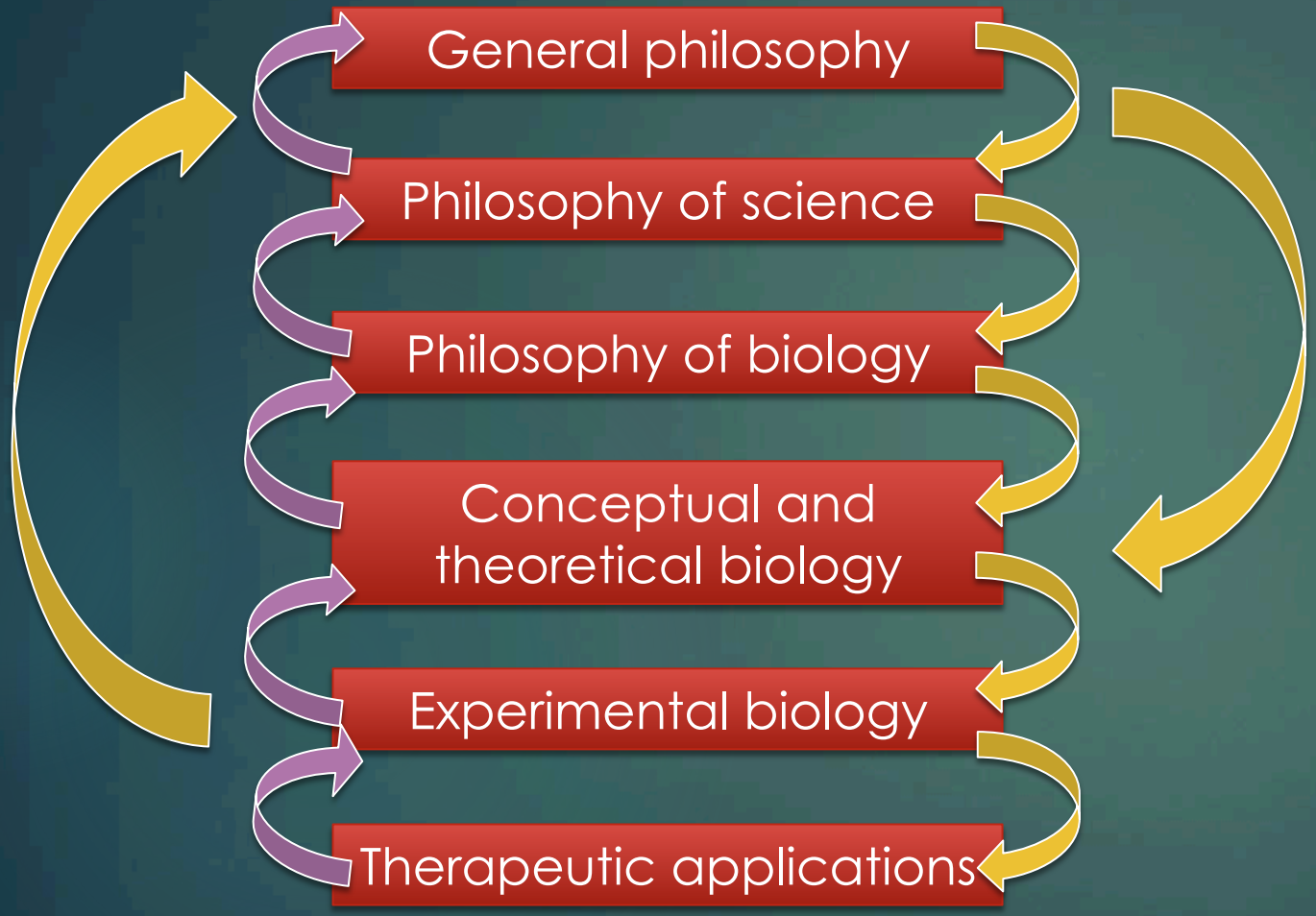
3. A philosophy of immunology aiming at a multilevel contribution

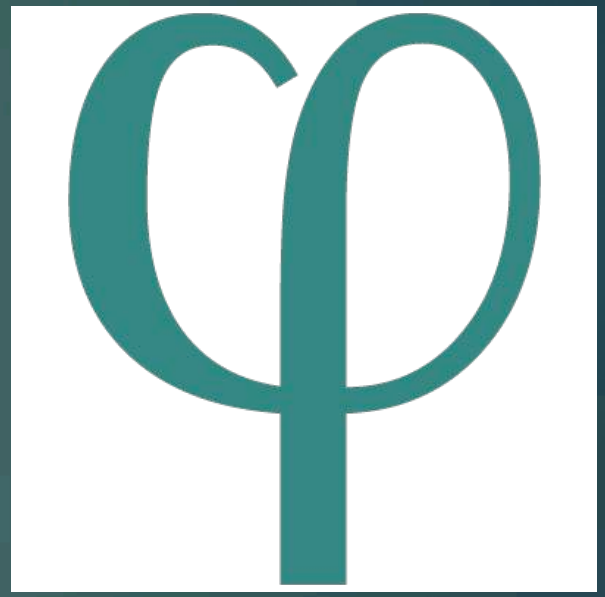
Levels of knowledge and interactions between them



- Possible "leaps" between levels
- No hierarchy

Ambition to contribute to all these levels (and their interactions)

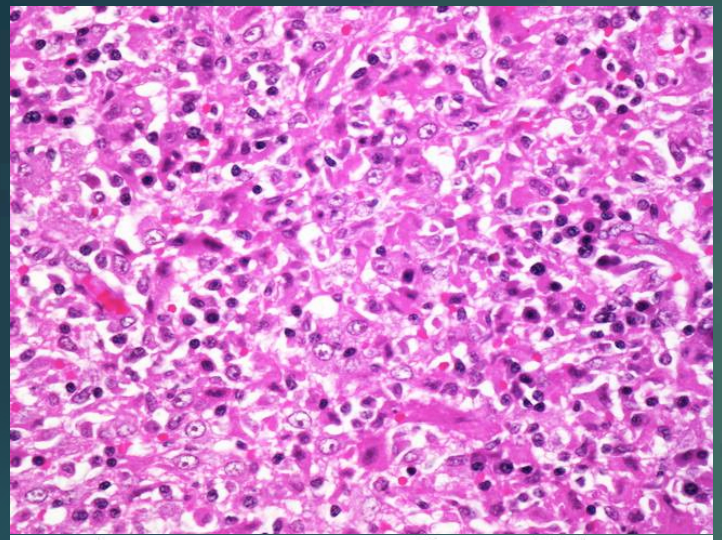


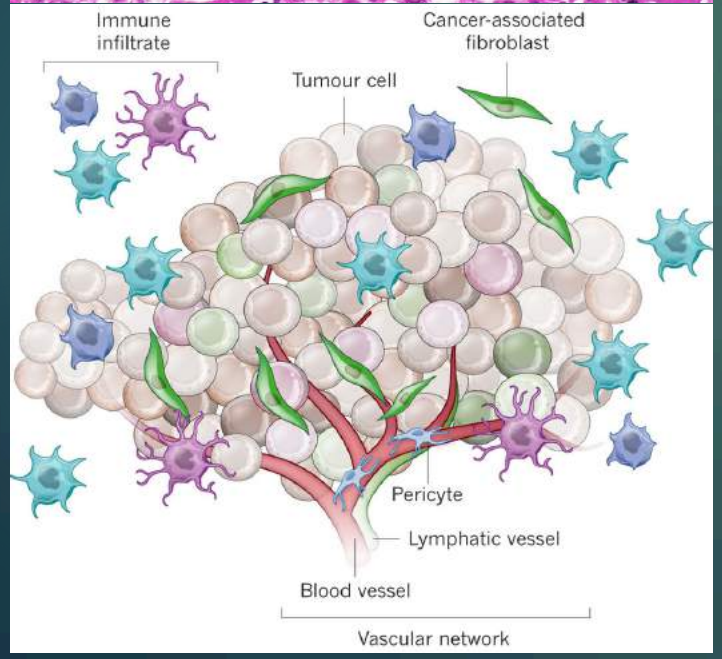


Ambition to contribute to all these levels (and their interactions)

General philosophy	Interactionist individuality
Philosophy of science	Interventionist philosophy of science
Philosophy of biology	Indispensability of immunity to understanding BI
Conceptual and theoretical biology	Discontinuity theory of immunity Re-definition of immunity as construction and repair
Experimental biology	Kinetics of IR IS in repair; IS in TME
Therapeutic applications	Modulation of IS in repair-associated disorders Promotion of "ecosystemic" medicine

Contributions to experiments





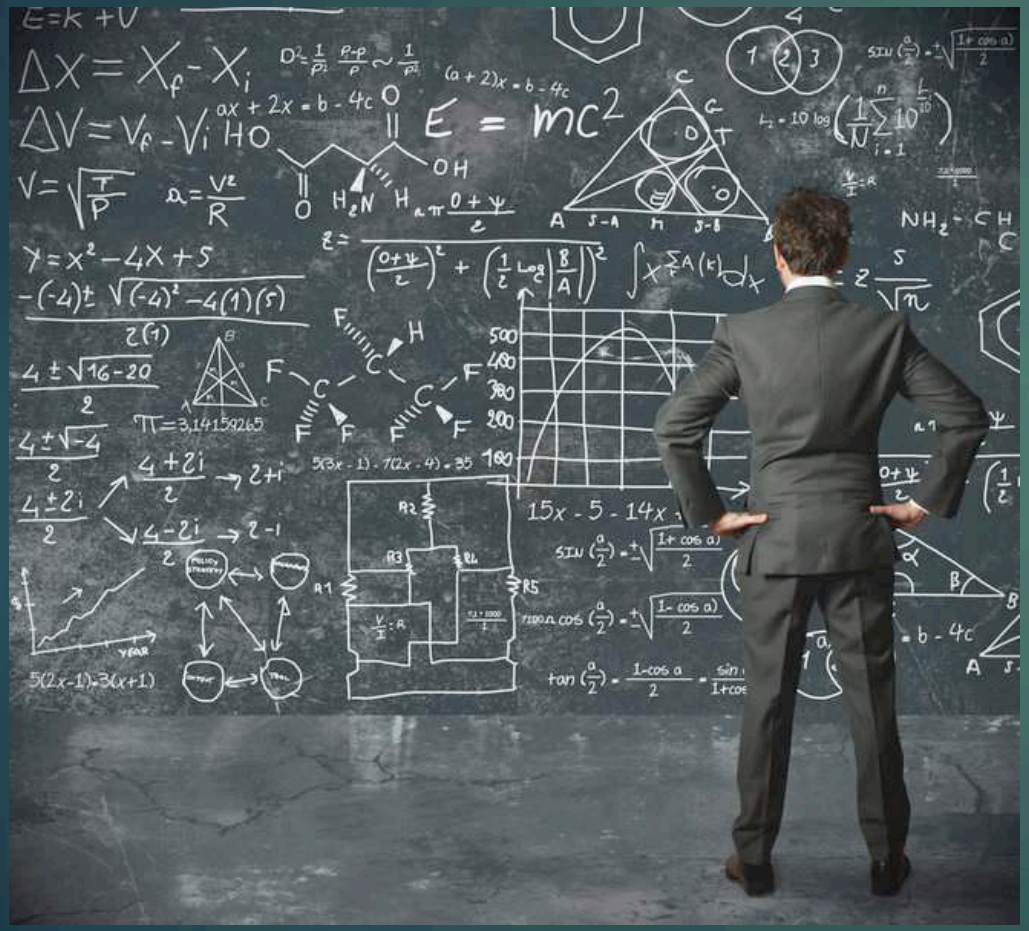
- Difficult and rare.
- **Some examples** of what we currently investigate with my group in the lab:
  - Are the mechanisms of immune-mediated tissue repair involved in **immune-promoted tumorigenesis**?
  - How different cell types **interact** in immune-mediated tissue repair? What is the role of **timing** 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

- **Truchetet M-E. & Pradeu T. (forthc.), Re-thinking the definition of immunity: robustness in tissue reconstruction, *Seminars in Immunology*.**
- **Du Pasquier L. & Pradeu T. (forthc.), How to define immune memory?, *Immunological Reviews*.**
- **Eberl G. & Pradeu T. (forthc.), Towards a general theory of immunity?, *Trends in Immunology*.**
- **Chiu L., Bazin T., Truchetet ME. , Schaeverbeke T., Delhaes L. & Pradeu T. (forthc.) Protective Microbiota: From Localized to Long-Reaching Co-Immunity, *Frontiers in Immunology*.**
- Guay A. & Pradeu T. (in press) Right out of the box: How to situate metaphysics of science in relation to other metaphysical approaches. Forthcoming in *Synthese*.
- Bich L. & Green S. (in press), Is defining life pointless? *Synthese*.
- **Hooks K.B. & O'Malley M. (2017) Dysbiosis and Its Discontents. *mBio*.**
- Ferner A. & Pradeu T. (eds., (2017) Special issue on "Ontologies of Living Beings", *PTPBio*,
- **Laurent P., Jolivel V., Manicki P., Chiu L., Cotin-Bordes C., Truchetet M-E. & Pradeu. T. (2017), Immune-Mediated Repair: A Matter of Plasticity. *Frontiers in Immunology*.**
- Pradeu T. (2017), Thirty years of Biology & Philosophy: Philosophy of which biology? *Biology & Philosophy*.
- **Moreau J-F., Pradeu T., ..., Franceschi C. (2017), The re-emerging role of ECM crosslinking in T cell mobility as a hallmark of immunosenescence. *Ageing Research Reviews*.**
- **Pradeu T. & Vivier E. (2016), The Discontinuity Theory of Immunity, *Science Immunology*.**

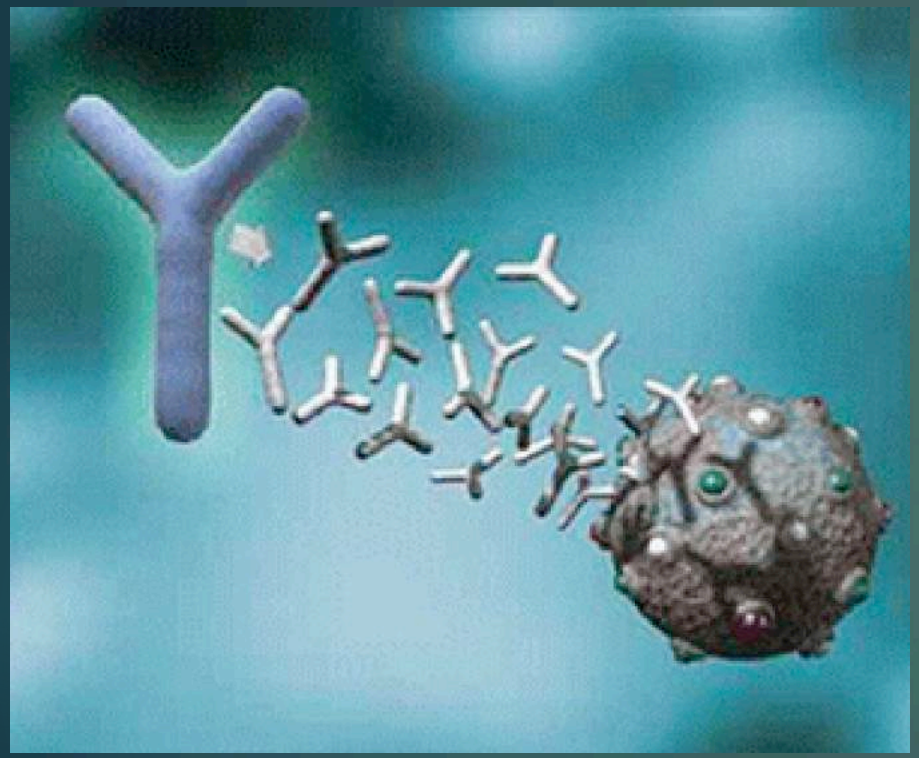
4. The virtues of philosophy *in* science

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.)

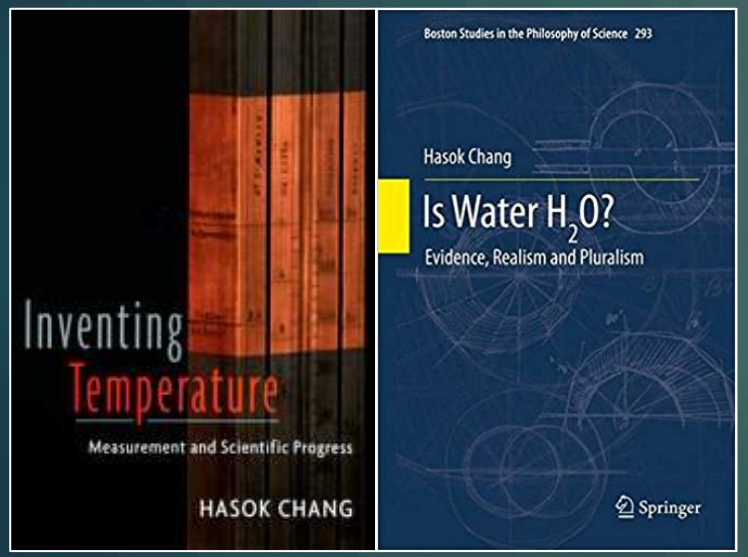
There is nothing new in "philosophy in science"!

- 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

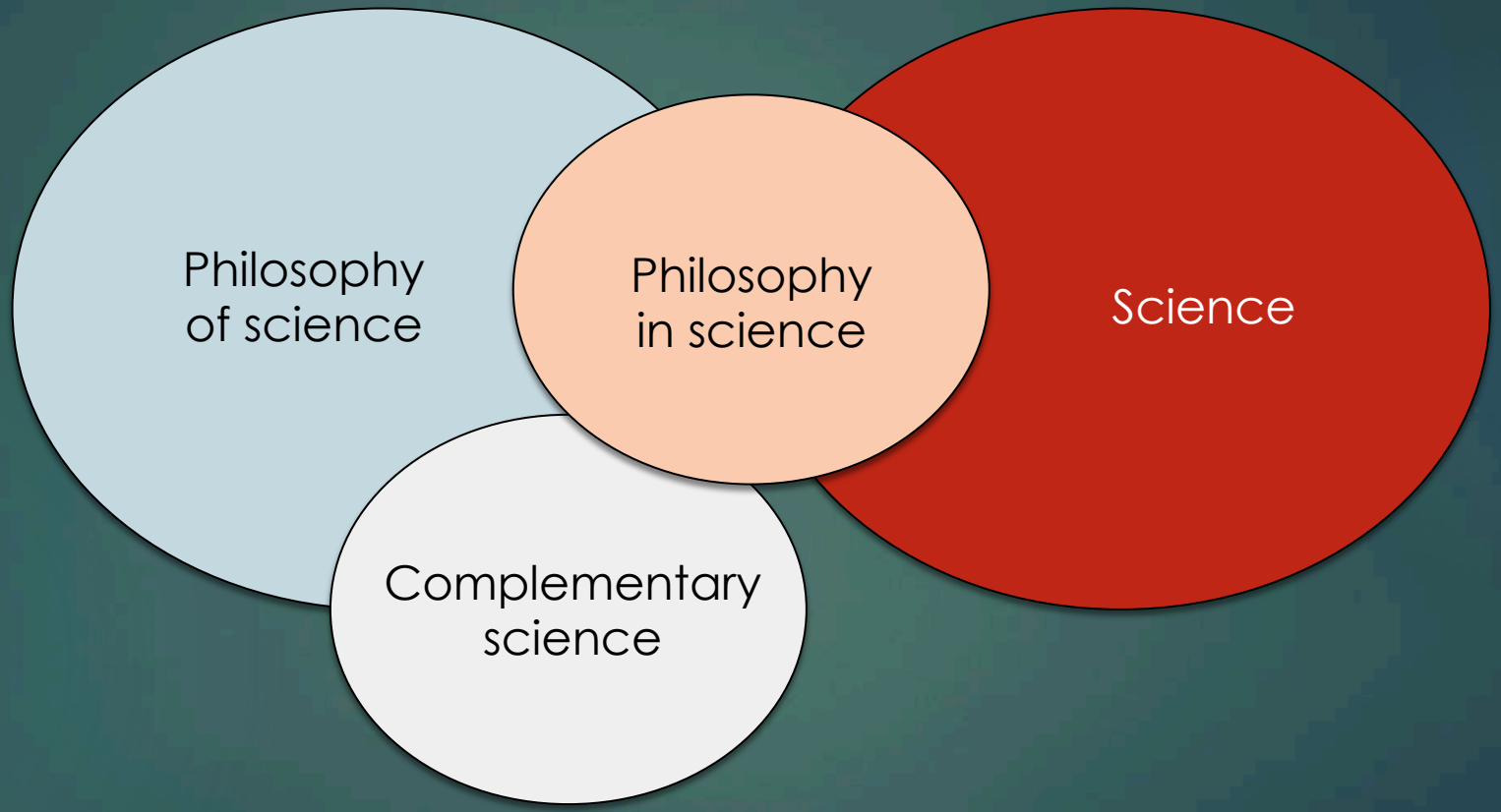
- Strong move in recent philosophy of science.
- Remains in most cases a description of science, not a contribution to science.

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.
- When? Kuhn: philosophers in period of crisis. In fact: philosophers for those who re-think their discipline.

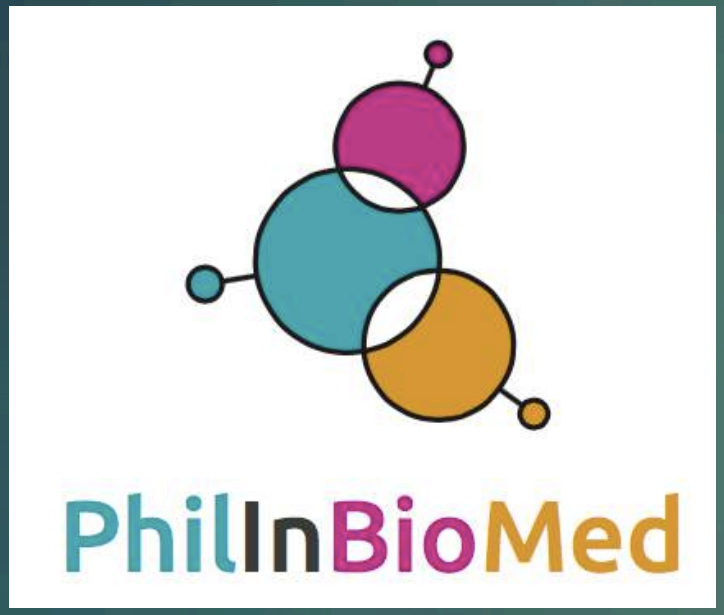
Philosophy of science & Philosophy in science



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



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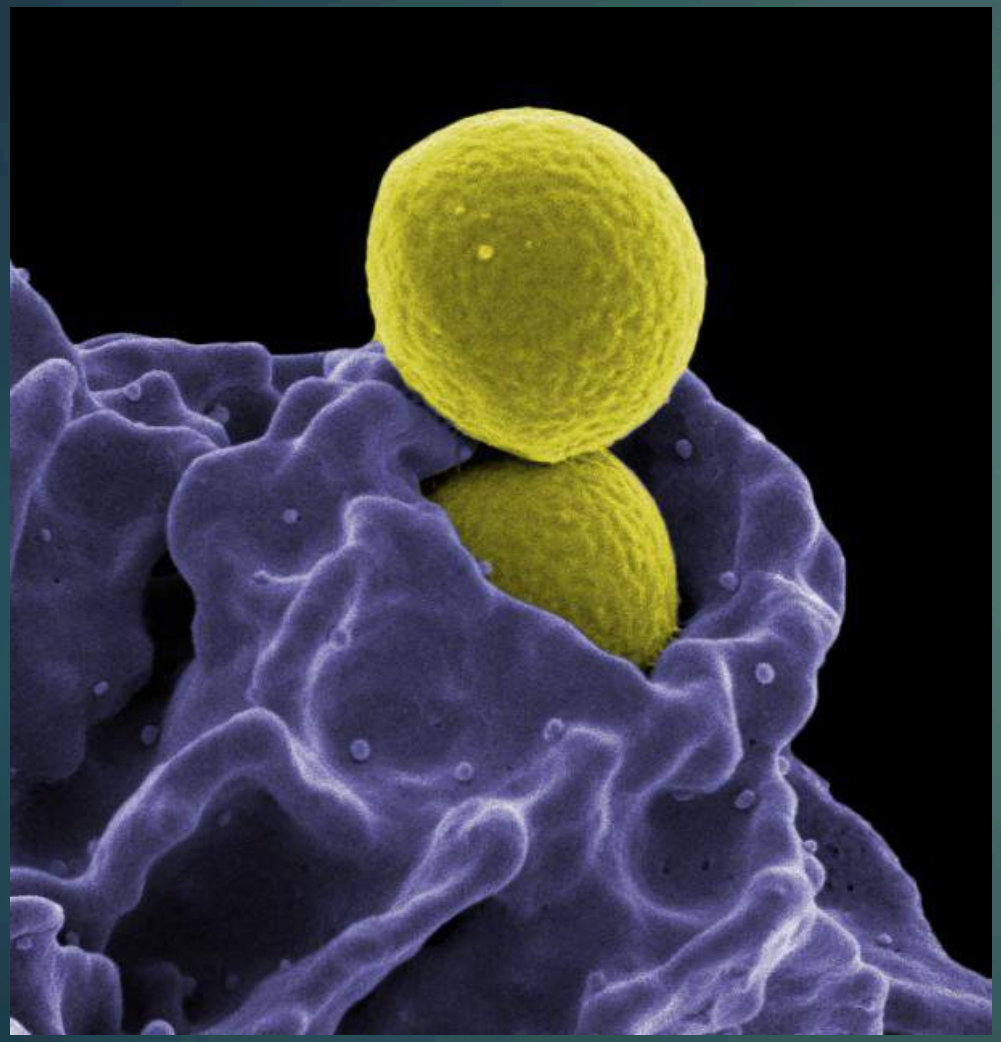
- **4 main guiding principles:**
  - ✓ Interventionism
  - ✓ "Embedded" philosophers
  - ✓ Co-writing of papers in both science and philosophy journals
  - ✓ Common reading groups
- **International network** of similar initiatives (Sydney, MBL, Cambridge, Exeter, etc.)

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.

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- https://www.immuconcept.org/conceptual-immunology/