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Autoreferát (teze) disertační práce

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Models and Modeling in the Biomedical Sciences

Modely a modelování v biomedicíně

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Introductory note

The thesis deals with several interrelated topics concerning the philosophy of scientific modeling in the context of biological and biomedical research, broadly construed. Scientific literature is notoriously loose when it comes to providing a precise clarification of some of the general concepts such as 'model'. Given that the goals of a scientific paper can be achieved perfectly well without dwelling too much on making the meaning of these general terms more precise, the vagueness should be of no concern. However, since one of the goals of philosophical analysis lies in unpacking such general terms, it must proceed with more care. Furthermore, because modeling is such an essential tool, one may benefit from sharpening the key concepts pertaining to this practice. Indeed, philosophers have long been interested in questions concerning how to characterize the practice of modeling, what models are and how they work. It should be noted that the existing range of topics related to modeling is too vast for any thesis to address and to provide an original contribution rather than a simple restatement or overview of existing views; therefore, a selection had to be made.

Basic biomedical research is, to a large extent, oriented toward studying mechanisms. It is therefore only natural that much of the thesis addresses the question of (1) modeling mechanisms and (2) mechanistic explanation. To learn about disease mechanisms, biomedical researchers also often rely on the use of animal models such as mouse models (3). Mechanisms, however, can also be studied using more theoretical apparatus in the form of simulations, as the case of agent-based modeling of the outbreak of SARS-CoV-2 illustrates (4). Although I primarily discuss case studies related to cancer research and cancer immunology, I also discuss immunology more generally and present a conceptual model of how to think about the immune system (5). In light of the COVID-19 pandemic and possible future ones, an adequate understanding of the immune system is required, and philosophy can be of assistance in that regard.

The work on the thesis has required the use of various methods of inquiry. In addition to the careful examination of the relevant philosophical literature, I have benefited from employing several empirical methods to inform the conceptual analysis (see Zach 2019 for an overview of a variety of such methods). In particular, I have benefited from interviewing scientists and from conducting a participant observation of the research practices during my visit to the ImmunoConcept lab, a research facility located in Bordeaux specializing on research in immunology and cancer.

In what follows, I outline the main claims of the thesis.

1. I propose a complementary account of scientific modeling – the experimentation-driven modeling account – using laboratory research in cancer immunology as a case study

The practice of scientific modeling has been characterized as an indirect strategy of scientific theorizing which happens in roughly three stages: scientists (i) construct a model which they then (ii) investigate and, finally, they (iii) compare it to the target phenomenon (Weisberg 2007, 2013). This view, which I call the *description-driven modeling (DDM) account*, has been distinguished from other, direct, ways of theorizing such as the practice of *abstract direct representation* (ADR). DDM has become widely accepted in the philosophical literature because it fits nicely with much of modeling practice, a fact that has been thoroughly documented on a vast array of examples.

Mechanistic models are an important class of models used in various fields of biological and biomedical sciences. The main claim of this chapter is that DDM fails to naturally account for much of the practice of mechanistic modeling and thus must be *complemented* by another account. Based on a case study of the research in cancer immunology, I propose the *experimentation-driven modeling (EDM) account*.

In particular, the case study concerns current research on the role of myeloid-derived suppressor cells (MDSCs) in facilitating the formation of a pre-metastatic niche. In other words, current research indicates that the metastatic organs undergo changes before the arrival of primary tumor cells (Liu and Cao 2016). Thus, the secondary site is actively being transformed in a complex dynamic process that gives rise to a pre-metastatic niche which ultimately leads to the establishment of a metastasis (Liu and Cao 2016). One of the key players implicated in establishing a pre-metastatic niche are myeloid-derived suppressor cells (MDSCs), a heterogeneous population of immature cells of myeloid origin activated under pathological conditions (Gabrilovich and Nagaraj 2009).

In presenting the case I draw on the use of empirical philosophy of science: participant observation in a cancer immunology research lab, interviews with cancer immunologists, and a review of scientific literature dealing with MDSCs and pre-metastatic niche formation. Following the research project of Elena Rondeau, a cancer immunologist, I describe several of the experimental methods used to generate results that are later used to construct a mechanistic model. In particular, I describe research practices concerning the use of cell cultures and mouse models, and a variety of assays pertaining to immunohistochemistry, visualization methods, and phenotyping by flow cytometry. Furthermore, I discuss studies that rely on inhibitory or excitatory experiments.

The case study allows for drawing general philosophical conclusions regarding the practice of modeling. In EDM, scientists integrate piecemeal experimental results into a mechanistic model which is often expressed in the form of a diagram. Just as DDM, EDM proceeds in several steps: scientists (i) propose to study a set of experimental systems that are assumed to capture some aspect of the target phenomenon and they investigate these systems using a variety of experimental methods; (ii) using the information obtained from experiments, they construct a mechanistic model; (iii) they compare the model to the target phenomenon.

Importantly, EDM maintains the key characteristic of indirectness. This is because scientists do not have direct access to the target phenomenon – the process of cancer metastasis. Rather, they choose to investigate much simpler experimental systems that are relatively easy to manipulate.

Yet, EDM differs from DDM in other respects. First, the model construction comes later in the process. Whereas in DDM they key aspect of scientific work concerns the investigation of the proposed model, in EDM the model is proposed as the result of the experimental investigation. In other words, the particular steps in which mechanistic models in cancer immunology are derived from experiments appear to differ from the steps in DDM. As previously noted, in DDM, the modeling process happens in roughly three stages: scientists first use model descriptions to construct a model as a stand-in for the target phenomenon (*model construction*); they then investigate the model to find out what it implies (*model analysis*); and finally, they compare the model results with the target phenomenon (*model comparison*). Thus, one of the differences is that whereas DDM begins by constructing a model, followed by its analysis, EDM's starting point is an experimental investigation which ultimately leads to model construction. However, Weisberg (2013, p. 74) notes that the stages of DDM do not necessarily occur in this rigid order as they may happen together or iteratively. Still, the order of steps does seem to be representative of much of the practice, setting it apart from EDM. Second, one may also wonder to what extent EDM and DDM are, in fact, distinct as both can clearly rely on experimental results. Model descriptions that give rise to models as per the DDM approach can be assumptions but also empirical data, among other things. Thus, the line between the two cannot be drawn on such terms. However, a closer inspection reveals an important difference not to be missed. EDM engages in the laborious processes of experimental data generation whereas DDM more often relies on pre-existing data. Thus, the kinds of expertise required are often very different. More importantly, the crucial difference lies in the crux of the research practices involved in the two modeling approaches:

while the crux of the work in DDM is the study of the model, in EDM the work is basically considered done once a model is proposed. In other words, DDM is best characterized by ‘playing around’ with a given model, and although models also serve cognitive purposes in EDM, e.g., to provide a comprehensive picture of the mechanism, EDM does not ‘play around’ with models. Conflating the two modeling approaches would thus obscure important epistemic differences in scientific practices.

There are also important differences between the two accounts with respect to the role of assumptions. In DDM, the assumptions (i.e., the model descriptions) define the model (i.e., the model system). In contrast, in EDM, the assumptions concern the extent to which the studied experimental systems can provide relevant information about the target, as well as the extent to which the experimental results are valid; they do not define the mechanistic model. Finally, while DDM fits the sociological dimension of modeling (Godfrey-Smith 2006), EDM does not. However, EDM is proposed as an account of qualitative mechanistic modeling which sets it apart from the sociologically salient field of quantitative modeling. Several other differences and similarities are also further discussed in the main text of the thesis.

Because experimentation is part and parcel of the EDM account, one could gain the wrong impression that any instance of experimentation amounts to modeling. One can run an experiment or even a series of experiments without piecing the results together into a mechanistic model. It is only when there is an effort to understand the mechanism responsible for the phenomenon of interest by running a series of experiments, the results of which are ultimately accounted for by developing a model, that we can speak of EDM. Experimentation on its own should not be conflated with modeling.

2. I argue against the objection that the mechanistic account of explanation fails to account for the practice of idealizing difference-making factors in models in molecular biology

The world in which we live is immensely complex. Indeed, its complexity vastly exceeds our capacity to grasp it in its entirety with all the exact detail in place. Nevertheless, scientists do more than a decent job of keeping the complexity in check by constructing models of selected phenomena that help us to understand, explain, predict and control various aspects of the world. To achieve this, models must be simple enough to facilitate insight into the phenomena. In the literature of the past several decades, much has been said about the nature(s) and function(s) of models. Many, though not all, authors prefer to speak of abstraction and idealization as examples of tools for introducing simplifications into models. Overall, models are commonly considered to be relatively poor in detail and often to provide distorted accounts of their target systems.

One set of papers that deals with the topic of abstraction and idealization often relies on a ready-made distinction. In the simplest terms, idealization is construed in terms of (deliberate) distortion, misrepresentation and/or falsehood and amounts to providing an inaccurate picture of the studied system, whereas abstraction concerns the omission of an (irrelevant) feature (Boone and Piccinini 2016; Chirimuuta 2014; Frigg and Hartmann 2020; Halina 2018; Levy and Bechtel 2013; Love and Nathan 2015). Some of the authors who use the distinction explicitly draw on another set of papers which aims to provide a more nuanced characterization of the terms by clarifying in what precise sense idealization may be thought of in terms of distortion, misrepresentation and falsehood, and abstraction in terms of omission of detail (Godfrey-Smith 2009; Jones 2005; Levy 2018; Mäki 1992; Portides 2018; Potochnik 2017). Naturally, some of the authors who develop accounts of abstraction and idealization then end up using them, or *vice versa*. For instance, Levy in Levy and Bechtel (2013) quoted above simply uses the distinction, referring to Jones (2005) and Godfrey-Smith (2009), while in his (2018) he develops a more nuanced account.

Importantly, abstraction and idealization have also been discussed in the context of specific philosophical debates such as that on the mechanistic account of explanation. In a recent paper, Alan Love and Marco Nathan (2015) have argued that the new mechanists' preferred view of explanation cannot account for the common practice of idealizing difference-making factors in models in molecular biology.

I scrutinize the analysis provided by Love and Nathan and I argue against their conclusion that the mechanistic account of explanation is in trouble. More specifically, I argue that their analysis paints a confusing picture for a number of reasons: it is interwoven with inconsistencies regarding (i) how they treat the one and the same modeling assumption, (ii) how they apply their preferred definitions, and (iii) how they formulate the core objection. Moreover, the assumptions that they present as idealizations can – instead, and perhaps more naturally – be accounted for in terms of abstractions. In the process, I also draw several general lessons for the debate on abstraction and idealization and its use. For one thing, I show that philosophers developing accounts of these notions often disagree among themselves with respect to a number of issues, meaning that the notions might not be as clear cut as generally believed. Relatedly, while the distinction between abstraction and idealization is relatively easy to spell out, it proves extremely tricky to adequately apply it in scientific practice. This may, in part, be due to the fact that the various existing accounts have been developed in different disciplinary contexts; and applying the distinction originally developed in one context to another may not be a straightforward process, for it may overlook important differences in epistemic practices characteristic of the respective disciplines. Finally, the arguments laid out in this chapter should also serve as a cautionary note to those who have embraced the objection to the mechanists, not realizing the fundamental issues underlying such criticism. More generally, philosophers may need to pay special attention when using the concepts of abstraction and idealization before these concepts can do any real work in a philosophical argument.

3. I describe and analyze the epistemic roles of similarity considerations in mouse models of cancer and I argue that by appreciating the epistemic complexities it is possible to shed new light on the debate on the similarity account of scientific representation

Much has been already written on many aspects of research which employs model organisms in order to investigate biological phenomena (Ankeny and Leonelli 2020). Predominantly, the philosophical scholarship has focused on the criteria that guide the choice of model organism, and on the justificatory efforts concerning extrapolative inferences from a model organism to a target system. Similarly, the concept of similarity has attracted significant attention in the context of the debate on scientific representation (Giere 1988; Weisberg 2013), with some attention given to discussing the more specific sense of similarity found in a particular disciplinary context (see, e.g., Sterrett 2017 on the concept of a physically similar system). Focusing on cancer research, and particularly upon cancer immunology, the arguments laid out in Chapter 3 contribute to the study of both modeling and similarity by mapping the practices which make use of mouse models.

More specifically, I concern myself with various kinds of mouse models such as the immunocompetent and immunodeficient transplantable models, genetically engineered models and humanized models. Providing the rudimentary understanding of what is going on in such research, I distinguish three research modes: *model selection*, *model creation*, and *model extrapolation*.

The selection of a mouse model is guided by the particular research question at hand, the similarity considerations, and a host of pragmatic and other factors. In model extrapolation, similarity considerations in one way or another are used to justify the extrapolative inferences of the preestablished features of the models. In this sense, much like in model selection, I argue that the similarities play a *passive* role. In contrast, model creation amounts to *actively* introducing changes so that a model is made to be similar to a certain degree and in certain respects to the studied phenomenon.

In general, while much has been written on the topic of model selection and model extrapolation, relatively little has been said about creating new animal models. Although the research modes are often intertwined in practice, they are both conceptually and temporally distinct, and as I argue in some detail, the concept of similarity plays different epistemic roles in each of the modes.

Clarifying these different roles proves crucial in an argument concerning scientific representation. Most generally, scientific representation has been characterized in terms of one thing standing for another. Thus, a scientific model is a representation of its target system because the model stands for its target. The question, then, concerns the nature of the standing-for relation. What makes a model stand for its target? A number of different accounts have been proposed: structuralist accounts (e.g., French 2003); the DEKI account (Frigg and Nguyen 2020); a variety of inferentialist and pragmatist accounts (Bolinska 2013; Contessa 2007; Knuuttila 2011; Suárez 2004); and the similarity account (Giere 2004; Godfrey-Smith 2006; Mäki 2005; Weisberg 2013), according to which scientists use models to represent their targets by utilizing similarities in certain respects and to certain degrees between a model and its target. Regarding the similarity account, exploiting the relevant similarities is what enables us to learn about the phenomenon of interest by studying its model instead. Despite its popularity in certain quarters, a wide range of objections have been leveled against the account. According to the objection addressed herein, one must distinguish between the concepts of representation and accurate representation, the latter – but not the former – possibly being grounded in the notion of similarity.

The analysis provided in this chapter shows, however, that the objection holds only to the extent that one is limited to discussing the evaluative aspect of modeling – model extrapolation. In contrast, model selection and model creation illustrate that similarity judgments play a key role in both establishing and maintaining the representational relation between the model and its target phenomenon.

4. I investigate the role of agent-based models of the outbreak of SARS-CoV-2 and the implications for informing policy decisions (based on joint work with Mariusz Maziarz)

Philosophical debates on modeling can also be applied to the COVID-19 pandemic. This chapter aims to assess epidemiological agent-based models—or ABMs—of the SARS-CoV-2 pandemic methodologically (Maziarz and Zach 2020, 2021). The rapid spread of the outbreak requires fast-paced decision-making regarding mitigation measures. However, the evidence for the efficacy of non-pharmaceutical interventions such as imposed social distancing and school or workplace closures is scarce: few observational studies use quasi-experimental research designs, and conducting randomized controlled trials seems infeasible. Additionally, evidence from the previous coronavirus outbreaks of SARS and MERS lacks external validity, given the significant differences in contagiousness of those pathogens relative to SARS-CoV-2.

To address the pressing policy questions that have emerged as a result of COVID-19, epidemiologists have produced numerous models that range from simple compartmental models to highly advanced agent-based models. These models have been criticized for involving simplifications and lacking empirical support for their assumptions. To address these voices and methodologically appraise epidemiological ABMs, AceMod (the model of the COVID-19 epidemic in Australia) is used as a case study of the modeling practice.

The example shows that, although epidemiological ABMs involve simplifications of various sorts, the key characteristics of social interactions and the spread of SARS-CoV-2 are represented sufficiently accurately. This is the case because these modelers treat empirical results as inputs for constructing modeling assumptions and rules that the agents follow; and they use calibration to assert the adequacy to benchmark variables.

Given this, the claim is that the best epidemiological ABMs are models of actual mechanisms and deliver both mechanistic and difference-making evidence. Consequently, they may also adequately describe the effects of possible interventions. Importantly, some of the key limitations of ABMs are discussed. There is always the risk that assumptions entertained in ABMs do not include all the key factors and make model predictions susceptible to the problem of confounding. Furthermore, considering that epidemiological ABMs account for not only biological determinants such as infectivity but also social interactions that differ across the globe, the quality of evidence from ABMs must be assessed on a case-by-case basis. In reaching policy decisions, ABMs should be understood as merely one piece of the puzzle subject to further re-evaluation with respect to value judgments. This is because alternative mitigation measures may disproportionately affect certain social groups. Therefore, the quality assessment aimed at identifying possible confounders that have been left out from a particular ABM should delineate the conflict of interest and the vested values related to the ABM and the mitigation measures that it supports.

5. I argue that to think about the immune system in terms of a strong or weak defense is to misconceive what the immune system is, what it does and why it sometimes fails; and I present a conceptual model of the immune system consisting of the features of contextuality, regulation, and trade-offs (based on joint work with Gregor Greslehner)

In their reflections on the COVID-19 pandemic, philosophers have shed light on a number of different aspects. However, immunology has yet to receive attention. Philosophy of immunology has only recently started to grow as a small field within philosophy of science (see Pradeu 2019; Swiatczak and Tauber 2020). Immunology can be an overwhelmingly complicated science, even for experts who have worked in the field for decades. However, the basic principles and underlying theoretical concepts are also a domain for philosophical reflections that benefit immunology, philosophy, and the consideration of how a wider audience of non-immunologists think about immunology.

The COVID-19 pandemic caused by the spread of SARS-CoV-2 naturally invites talk of a host defense against a foreign invader, a pathogen, giving rise to the idea that the stronger the defense against the pathogen (the foreign 'non-self'), the better for the host (the 'self'). This idea is further illustrated by the benefits of boosting one's immunity by vaccination, or the communication coming from some health agencies such as the CDC (2021) stating that immunocompromised individuals possess weakened immunity, which is a risk factor. However, such a construal of immunity is insufficient to account for many of the immune system's functions which include tissue repair, the maintenance of homeostasis, the clearance of debris, or a role in development in addition to defense. Furthermore, all these functions – including defense – are, in fact, also carried out by non-immune cells, including microbes. Thus, the immune system must be integrated into other physiological systems to account for various functions. Finally, the narrow construal of immunity fails to account for many important features of the immune system.

Many features of COVID-19 painfully remind us of several issues concerning the immune system and raise important questions, including some which extend beyond COVID-19. These issues and questions include, but are not limited to: the contextuality of the immune response; the trade-off between fighting off an infection (immunity) and in so doing causing collateral damage (immunopathology); the two defense strategies, i.e., clearing the pathogen (resistance) and decreasing the susceptibility of the host to tissue damage (disease tolerance); the importance of immune regulation; and questions going well beyond the narrow conception of immunity as a defense system.

In this chapter, three features of the immune system noted above are addressed: contextuality, regulation, and trade-offs.

Contextuality. The immune system, i.e., a vast network of interacting parts that can be carved up in multiple ways, is in fact constantly interacting with its environment, with the outcome of these interactions being context-dependent through and through. Furthermore, it is important to point out that such contextuality comes in many layers. Which immune function is triggered depends on the particular situation, driven by the integration of various signals and immune mediators such as cytokines. One and the same element often fulfills different functions (interferons in inflammation and homeostasis); pathogenicity is a complex and dynamic relation, and it is a function of traits that are intrinsic not only to the virus but also to the host; being immunocompetent, too, is a contextual feature, and so are some kinds of immunodeficiency.

Regulation. Malfunction of the immune regulatory mechanisms – immune dysregulation – is at the heart of many pathologies. Examples include cross-regulation of types of responses, delayed responses due to the presence of autoantibodies against crucial mediators of immune responses, and the changes in the aging human organism, among countless others.

Trade-offs. The workings of the immune system exhibit numerous trade-offs on multiple levels of organization. While certain responses are beneficial in certain contexts, they are detrimental in others (e.g., immunological tolerance in pregnancy as opposed to cancer); an important trade-off occurs between immunity defined as an inflammatory response and the level of immunopathology resulting from such inflammatory response; inducible disease tolerance mechanisms work at the expense of normal tissue function; manipulating the immune system often results in unwanted responses (e.g., checkpoint inhibitors in cancer immunotherapy lead to autoimmune disease in some patients); or the particular genotype that confers benefits against some X, while increasing susceptibility to some Y (e.g., HLA alleles in HIV and autoimmunity).

This tripartite view allows us to take a broader perspective on many aspects of COVID-19 and achieve a better understanding of the immune system in general. Using this conceptual model, it is also possible to draw attention to misleading metaphors originating from the idea that the immune system is primarily a defense system to fight pathogens.

War-like metaphors, such as defending the ‘self’ against pathogenic invaders, continue to shape how many scientists and physicians think about the immune system and how immunology is being communicated to the wider public. Since metaphors have their uses and abuses, it is important to see how they guide one’s intuitions and how we think about the immune system. Using the above conceptual model, it is possible to provide a non-exhaustive categorization of what the otherwise ill-defined notions of ‘strong’ or ‘weak’ immunity might mean, and to argue that some of the (outdated or questionable) distinctions and metaphors of self, danger, defense, and strength of the immune system or response, have led to misconceptions, limiting our understanding of the immune system.

It is true that there does seem to be a perfectly legitimate *descriptive* sense in speaking of immune response when defined as pertaining to a quantitative measurement of certain immune features: e.g., assays allowing measurements of cytokine production, the number of cells, the titers of neutralizing antibodies as a proxy for protective immunity, binding affinities, and so on. Overall, however, the talk of a strong/weak immune system or response mischaracterizes the workings of the immune system in the following way:

(i) *Normative connotation*. Strong defense or the idea of boosting immunity may be viewed as desirable, but in many cases it may lead to pathology or come at a cost (e.g., immunopathology).

(ii) *Paradoxical connotation*. Immunodeficiency invites the intuition that the issue is one of a weak response. However, the same immunodeficiency could also concern an issue of a strong response (e.g., IPEX) and it is not clear which notion should apply.

(iii) *Not applicable because not amendable to change*. Thinking in terms of a continuum between strong and weak immunity and the idea of boosting immunity is sometimes invalid (e.g., neonatal thymectomy).

(iv) *Lack of meaning conveyed*. Many phenomena and functions of immunity cannot be meaningfully captured by these notions (e.g., homeostasis).

(v) *Failure to account for what the immune system is, what it does and why it sometimes fails*. Rather than being in a steady state until an occasional threat emerges, the immune system is constantly active in maintaining various functions, including functions other than defense. All immune-related phenomena require a contextual understanding; otherwise, one would fail to understand why a phenomenon may be desirable but also detrimental (e.g., in immunological tolerance, or the trade-off between immunity and immunopathology). The notions of strong/weak immunity also give the wrong impression that the immune system can be described along this (one) dimension.

As a result, we need to move away from viewing the immune system narrowly as a defense system, and to drop related notions that prevent us from achieving adequate understanding. The conceptual clarification of these matters showcases the use of philosophy of science in the quest for a better understanding of the immune system.

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Academic activities

Employment

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2019 (October – December) Research visitor at the ImmunoConcEpT lab, CNRS UMR 5164, University of Bordeaux, host: Dr. Thomas Pradeu
2018 (August - November) Research visitor at the Centre for Philosophy of Social Science ('TINT'), University of Helsinki, host: prof. Uskali Mäki
2017 (September - December) Research visitor at the Centre for Philosophy of Natural and Social Science (CPNSS), London School of Economics, host: prof. Roman Frigg

Publications

Papers in peer-reviewed journals

2021

- 2 papers currently under review
  - Understanding the immune system in times of COVID-19 and beyond: Misconceptions and metaphors (with Gregor Greslehner) (*History and Philosophy of the Life Sciences*, IF: 0.87)
  - Revisiting abstraction and idealization: How not to criticize mechanistic explanation in molecular biology (*European Journal for Philosophy of Science,* IF: 0.86)
- **Assessing the quality of evidence from epidemiological agent-based models for the COVID-19 pandemic** (with Mariusz Maziarz). *History and Philosophy of the Life Sciences* 43 (1), 1-4 (IF: 0.87), https://doi.org/10.1007/s40656-020-00357-4

2020

- **Agent-based modeling for SARS-CoV-2 epidemic prediction and intervention assessment. A methodological appraisal** (with Mariusz Maziarz). *Journal of Evaluation in Clinical Practice* 26 (5), 1352-1360 (IF: 1.68), https://doi.org/10.1111/jep.13459

2019

- **Conceptual Analysis in the Philosophy of Science**. *Balkan Journal of Philosophy* 11 (2), 2019, s. 107-124, https://doi.org/10.5840/bjp201911212

2017

- **Scientific realism as spiritual cultivation** (in Czech). *Filozofia* 72 (5), 2017, p. 381-391.
- **Selective realism and the caloric theory of heat** (in Czech). *Filosofický časopis* 65 (1), 2017, p. 77-95.

Editorial work

- Guest editor (with Elay Shech and Melissa Jacquart) on a special issue **"Idealization, Representation, Explanation Across the Sciences"** of the journal *Studies in History and Philosophy of Science* (IF: 1.21)

Reviews and reports

- **Axel Gelfert: How to do science with models: A philosophical primer**, *Organon F* 24 (4), 546-552, 2017.
- **Perspectives on Explanation**, 18-19 May, *The Reasoner* 11 (6), 30-31, 2017.

Translation

- Modely versus evidence, etikaepidemie.cz

Chapter in a collective monograph

- Illogical society (in Czech). In: Rynda, I. (ed.) (2015): *Krize: Společnost, kultura a ekologie*. Praha: Togga, p. 87-103.

Grants and scholarships

- **2019 – 2021**, Simplifying Assumptions and Noncausal Explanations, **Czech Science Foundation** (GA ČR 19-04236S) (co-PI with Lukas Zamecnik from Palacky University Olomouc)
- **2019**, **EPSA Fellowship** (for research visit to ImmunoConcept lab, CNRS & University of Bordeaux)
- **2019**, **French government scholarship** (for research visit to ImmunoConcept lab, CNRS & University of Bordeaux)
- **2018**, **Scholarship "Hlávka foundation"**
- **2018**, The Issue of Scientism, Internal grant of the Faculty of Arts, Charles University (**SVV funded project**)
- **2018**, **EDUFI Fellowship** (for research visit to TINT, University of Helsinki)
- **2017**, **Anglo-Czech Educational fund** (for research visit to CPNSS, LSE)
- **2017 – 2019**, Philosophical aspects of scientific models, Charles University Grant Agency (**GAUK** project no. 66217) (principal investigator)
- **2017 – 2018**, Principles of naturalizing philosophy of science, Internal grant of the Faculty of Arts, Charles University (**VG FF UK**) (principal investigator)

Conference talks (international only)

2021

- "Epistemic roles of similarity considerations in mouse models of cancer", *8th Biennial Conference of the European Philosophy of Science Association* (EPSA21), Turin (Italy), 15-18 September 2021 (online?)
- "Epistemic roles of similarity considerations in mouse models of cancer", *British Society for Philosophy of Science Annual Conference* (BSPS2021), Kent (UK), 7-9 July 2021 (online)
- "How to think about the immune system in times of COVID-19 and beyond: why stronger isn't always better and other misleading metaphors", *9th Philosophy of Medicine Roundtable*, Michigan State University (USA), 27-30 June 2021 (online)
- "Modeling in Biomedicine: Extending the notion of models", *Third conference of the East European Network for Philosophy of Science (EENPS 2021),* Belgrade (Serbia), June 9-11 2021 (online)
- "How to think about the immune system in times of COVID-19 and beyond: why stronger isn't always better and other misleading metaphors", *Philosophical Perspectives on Covid-19*, 10-13 May 2021 (online)
- "Building Mechanistic Models in Cancer Immunology: Towards a Complementary Account of Modeling" (poster), *27th Biennial Meeting of the Philosophy of Science Association (PSA2021)*, Jan. 22, Jan. 29, and Feb. 5, 2021 (online)

2020

- "Modeling in Cancer Immunology: A Complementary Account", *Bordeaux-Sydney Workshop on Philosophy of Biology and Biomedicine*, 23-24 November 2020 (online)
- "Are ABM epidemic models the models of actual mechanisms?" (jointly with M. Maziarz), *Jagiellonian University*, 5 May 2020 (online)

- Representing cancer in humans: Reviving the similarity account of scientific representation, *2nd SURe Workshop*, Atlanta (USA), 12.-13.3.2020

2019

- Theoretical models as abstract objects?, *4th POND Conference*, Barcelona (Spain), 26-27 September 2019
- "Revisiting abstraction and idealization in molecular biology", *7th Biennial Conference of the European Philosophy of Science Association* (EPSA19), Geneva (Switzerland), 6.-9.9.2019
- Understanding metabolic regulation: A case for the factivists, *16th International Congress of Logic, Methodology and Philosophy of Science and Technology (CLMPST 2019)*, Prague (Czech Republic), 5-10 August 2019
- "Revisiting abstraction and idealization in molecular biology", *British Society for Philosophy of Science Annual Conference* (BSPS 2019), Durham (UK), 17.-19.7.2019
- "The case of mechanistic explanation in molecular biology: abstraction or idealization?", *International Society for the History Philosophy and Social Studies of Biology biennial meeting* (ISHPSSB 2019), Oslo (Norway), 7.-12.7.2019
- "On Abstraction and Idealization in Molecular Biology", *workshop Idealization Across the Sciences*, Prague (Czech Republic), 12.-14.6.2019
- "Idealization and understanding with diagrammatic biological models", *Third International Conference of the German Society for Philosophy of Science (GWP2019)*, Cologne (Germany), 25.-27.2.2019

2018

- "Scientific understanding and the facticity condition", *IX Conference of the Spanish Society for Logic, Methodology and Philosophy of Science (SLMFCE)*, Madrid (Spain), 13.-16.11.2018
- "A case for factive scientific understanding" (poster), *26th Biennial Meeting of the Philosophy of Science Association (PSA2018)*, Seattle, WA (USA), 1.-4.11.2018
- "Mechanistic explanation in agent-based modeling", *Joint European Network for the Philosophy of the Social Sciences and Philosophy of Social Science Roundtable Conference*, Hannover (Germany), 30.8.-1.9.2018
- "There is no (special) problem of ontology of theoretical models", *Fourth Annual Conference of the Society for Metaphysics of Science (SMS4)*, Milan (Italy), 22.-24.8.2018
- "Similarity in practice", *Seventh Biennial Conference of the Society for Philosophy of Science in Practice (SPSP7),* Ghent (Belgium), 29.6.-2.7.2018
- "Scientific representation: Resituating the similarity account", *Second conference of the East European Network for Philosophy of Science (EENPS 2018),* Bratislava (Slovakia), 20.6.-22.6.2018
- "Mechanistic explanation in agent-based modeling" (poster), *11th MuST conference in Philosophy of Science: Models of Explanation,* Turin (Italy), 11.6.-13.6.2018
- "Similarity judgments and scientific representation", *Representation in Science*, Prague (Czech Republic), 28.-29.5.2018
- "Factive understanding with model sketches", *Explanation and Understanding*, Ghent (Belgium), 23.-25.5.2018
- "Minimal models, representation, and explanation", *Models and Simulations 8,* Columbia, SC (USA), 15.-17.3.2018

2017

- “Pluralism and minimal models" (poster), *What to make of highly unrealistic models?*, Helsinki (Finland), 12.-13.10.2017
- “Against the direct fiction view of scientific models”, *Sixth Biennial Conference of the European Philosophy of Science Association 2017*, Exeter (United Kingdom), 6.-9.9.2017
- “Against the direct fiction view of scientific models”, *Ninth European Congress of Analytic Philosophy*, Munich (Germany), 21.-26.8.2017
- “Conceptual analysis in philosophy of science”, *Triennial Conference of the Italian Society for Logic and Philosophy of Science*, Bologna (Italy), 20.-23.6.2017
- “Modifying the fiction view of scientific models”, *Fifth Annual Meeting of the Nordic Network for Philosophy of Science*, Copenhagen (Denmark), 20.-21.4.2017
- “Why the fiction view of scientific models is not your enemy”, *Scientific contents: Fictions or abstract objects?*, Santiago de Compostela (Spain), 26.-27.1.2017

2016

- “Naturalized philosophy of science: Two accounts of the method of conceptual analysis”, *Third Lisbon International Conference on Philosophy of Science*, Lisbon (Portugal), 14.-16.12.2016
- "Science and scientism“, *The Inaugural Conference of the East European Network for Philosophy of Science (EENPS 2016)*, Sofia (Bulgaria), 24.-26.6.2016

Invited talks

- “Mouse Models of Cancer: On Representation and Similarity”, *EENPS Online Seminar*, 1.4.2021 (online)
- “Pluralism in Philosophy and Science: Lessons from an Immunology Lab”, *CogPhi 2021 Workshop: Pluralism in Science & Philosophy*, Lund (Sweden), 31.3.2020 (online)
- “Mouse models in cancer immunology: An analysis of the epistemic roles of similarity judgments” (in Czech), Matej Bel University in Banská Bystrica (Slovakia), 3.3.2021 (online)
- “Scientific modeling via abstraction and idealization”, Trattenbach-Jilska seminar, Prague (Czech Republic), 13.12.2018
- “Philosophy of science then and now: The rise of the mechanisms and the practical turn”, Olomouc (Czech Republic), 6.12.2018
- “Abstraction and idealization in scientific modeling”, Pilsen (Czech Republic), 30.11.2018
- “Factive understanding with simple models”, Philosophy of Science seminar, TINT, Helsinki, 22.10.2018
- “Applying pretense to scientific models. Its merits and limits”, *XIII. Prague Interpretation Colloqium,* Prague (Czech Republic), 23.-25.4.2018

Organizing activities

- International conference “*Conceptual and Methodological Aspects of Biomedical Research*”, Prague (Czech Republic), 28-30 October 2020 (online)
- International workshop “*Ernst Mach Workshop 9: Non-Causal Explanation in Physics*”, Prague (Czech Republic), 16-17 September 2020 (online)
- Congress secretary and member of the LoC for the “*Congress on Logic, Methodology, and Philosophy of Science and Technology*” (CLMPST 2019), Prague (Czech Republic), 5.-10.8.2019

- International workshop “*Idealization Across the Sciences*”, Prague (Czech Republic), 12.-14.6.2019
- International workshop “*Representation in Science*”, Prague (Czech Republic), 28.-29.5.2018
- International workshop “*Perspectives on Explanation*”, Prague (Czech Republic), 18.-19.5.2017

Reviewer for:

- Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences
- Perspectives on Science
- Filozofia
- Filosofie dnes

Membership

- **European Philosophy of Science Association** (EPSA): elected student representative (with Agnieszka Proszewska) to the steering committee (2019-2021)
- **East European Network for Philosophy of Science** (EENPS): elected member of the steering committee (2020-2024)
- **Society for Philosophy of Science in Practice** (SPSP): Newsletter Team
- **Philosophy of Science Association** (PSA)
- **International Society for the History, Philosophy, and Social Studies of Biology** (ISHPSSB)
- **British Society for Philosophy of Science** (BSPS)