Book Review

Edited by Jordan Mansell

Alfred I. Tauber, *Immunity: The Evolution of an Idea* (New York: Oxford University Press, 2017), 328 pages. ISBN: 9780190651244. Hardcover: $78.00, Paperback $39.95.

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In his fourth work on the philosophy of immunity, Boston University's Alfred I. Tauber continues to explore the concept of immunity and how it affects the discipline of immunology and the broader biomedical sciences. Synthesizing philosophical thoughts and publications on biological immunity, Tauber describes a concept of immunity that goes beyond an organism simply defending itself from attack by pathogens.

In six chapters, the author sketches a philosophical skeleton on which to hang the accumulating fleshy experimental evidence that the human immune system is more than a system that seeks out and removes problematic "foreign" organisms and material. Tauber argues that this view of immunity is overly simplistic; he suggests instead that the immune system is an information-processing system that helps an "individual" — a highly topical word in the context of this book — interpret the world around them. In fact, Tauber goes further again and suggests that humans should really be considered a "holobiont": an organism made up of both the parts that we conventionally think of as "self" (i.e., organs, tissues, and individual cells) and the colonizing organisms that we normally think of as being "non-self," such as the gut microbiota, which is an increasingly exciting field of biology.

The adoption of microbiota as an important aspect of human physiology has gained a huge amount of attention in recent years, with therapies aimed at altering its composition and function showing great promise for diseases such as *C. difficile* infection and inflammatory bowel diseases. The rejection of the "self versus non-self" concept of immunity is the book's central theme, and, fittingly, its final passages contain a thought-provoking argument that immunology should rethink itself as an environmental science.

Immunity: The Evolution of an Idea begins by setting out the historical framework for the subsequent arguments. Although repetitive at times, the opening chapters provide an excellent and thoroughly readable basis from which to understand the more weighty philosophical questions posed later in the book. The author describes the origins of immunology and the development of two distinct schools of thought in the nineteenth century. The first, largely dismissed at the time, belonged to Élie Metchnikoff. He proposed that phagocytes, which engulf "foreign" or "external" objects, act as active agents of immunity via the causation of inflammation. This implied that phagocytes were making an autonomous judgment as to what was to be ingested or not and thereby defining the limits of organismal identity.

As Tauber tells it, the metaphysical implications of Metchnikoff's ideas of agency were thought to be too great a speculative leap, and more solid and measurable scientific physical/chemical interpretation became dominant, although Metchnikoff's ideas were later validated, including being awarded a Nobel Prize. By "agency," Tauber means the philosophical idea that a given agent (a cell in this instance) can act deliberately in response to a particular environment.

As Tauber describes it, the concept of agency returned to immunology when Mac Burnet introduced the word "self" into the immunological lexicon in 1940. This term implied that there must also be a "non-self" for an immune system with agency to defend against (such as invading bacteria or viruses) and that in some cases there must be "tolerance" to explain the enormous gray area that was left (including the essential bacteria that reside in the gut and do not elicit an immune response).

Tauber highlights an important issue at this juncture, namely, that all these words suffer from polysemy — the coexistence of many possible meanings — which is a theme explored more in subsequent chapters. He argues that although this ambiguous terminology has been epistemologically and practically useful, allowing major advances in our understanding of immunology,

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it is also nebulous and ultimately limiting to the scope of the field: it draws an insular circle around the "self," and this limits how "the self" can be understood. For instance, the strict interpretations of the metaphor require changes, or have been challenged, in instances in which self is treated as non-self — for example, as occurs in autoimmune diseases, in which, to quote the author, "the very distinction of self vs. non-self implodes." The result, according to Tauber, is a conceptual minefield when it comes to how the immune system treats events such as pregnancy and microchimerism.

These arguments are well reasoned, although perhaps the author is slightly dismissive of the progress made in immunology using these words and concepts. For instance, our understanding of the selection of correctly functioning T cells in the thymus still broadly fits in to this paradigm of "self" versus "non-self." In reply, Tauber would likely argue that this metaphor has brought us this far, but it is now insufficient to advance our understanding further — and I believe the book is persuasive in this respect.

With the background neatly presented for the reader and the author's case against the "self versus non-self" concept of immunity articulated, the book shifts from relatively accessible historical perspectives to more weighty philosophical discussions in an admirable attempt to reconceptualize the way we think of the immune system in the future.

To do this, Tauber goes to a great deal of trouble to bring the reader through the issues concerned with defining the "immune self" and the "individual" and where their boundaries may or may not lie. He describes a philosophical spectrum of possible definitions of immune selfhood, beginning with the most fixed and preordained definition, the "implicit self," through to the more fluid "emergent self": a non-fixed entity that is continuously being redefined by immune surveillance and emerging information. This last definition is a jumping-off point for the reader toward the author's conception of immune selfhood, as a changeable and shifting understanding of what the "self" is and how it interacts with the external "non-self" environment.

However, this does not appear to go far enough, and Tauber introduces us to the origins of the more complex network theories that disregard the concept of the self entirely. For example, in Niels Jerne's network model, the "self" is not conceptually invoked at all, and immunity is simply a complex network that only acts when a balance in the network is disturbed. This model was largely dismissed for a number of reasons, but in the 1990s, it became clear that "self versus non-self" was insufficient to explain autoimmunity and tolerance, the latter having been experimentally proven to be an active process rather than simply a passive silence that had been unclear until that point. Attempts were made to build on Jerne's network and describe the system "at rest," but they were initially unsuccessful, for various technical and conceptual reasons outlined in the book.

At this end of the spectrum is where Tauber starts to describe his own ideas on immunity as an ecological function. The arguments are, in my opinion, highly nuanced and make for thought-provoking reading. Briefly, the author outlines ingredients for his concept of a spectrum of immunity: three cardinal principles for hypothetical immune regulation: context, connectivity, and collective specificity. These ingredients are useful for understanding the author's arguments, and they are broadly well presented and have both experimental and theoretical evidence in their favor. The author also flirts with an analogy at this stage, using two characters (Adolf the Alligator and Sally the Squirrel) to illustrate the extreme ends of his spectrum, which makes for entertaining and informative reading.

Tauber's model is interesting and builds on much philosophical and theoretical work, and it harnesses the new experimental evidence that rapidly improving technology is allowing in the field of immunology (including next-generation sequencing). The model, in which the cells of the immune system can be considered part of the body's information-processing system, much like the nervous system, does not fully explain some concepts (such as the perennial issue of tolerance), but it is a conceptual leap that helps give a framework in which we can consider some of the discoveries that have been made in recent years. This is particularly true in the context of the microbiota: the vast milieu of microorganisms that inhabit the body's surfaces, whose transpiring are crucial for the function of their mammalian hosts. Understanding immunity simply as defense fails utterly to do justice to the wonderful homeostatic relationships that are being uncovered, and Tauber's work makes a clear and well-reasoned argument in favor of the holobiont mentioned earlier.

If a criticism can be leveled at this text, it is that it may be inaccessible for readers who are unfamiliar with philosophy and the style in which philosophy is written. However, I make this criticism because I believe that the ideas contained within are important, and I hope to see them widely engaged with by scientists and clinicians. These ideas may help shape future approaches to

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multiple therapeutic areas (especially those closest to the "self versus non-self" paradigm such as transplant biology and autoimmune diseases), and related health care policies, although I suspect this will happen slowly as the experimental evidence accumulates. Consequently, this book may be of interest to researchers studying how the evolving understanding of immune function and its influence on disease influences future policy considerations.

Furthermore, the philosophical discussion of self versus non-self, as well as the different models used to palpate these concepts, may be of interest to social scientists studying the concepts of agency, self, and identity.

This book is a real departure from the immunology texts that I interact with in my day-to-day work, and it has opened my eyes to a larger body of philosophical questions relevant to the field. It requires investment, but I found it to be worth the time. With that caveat in place, I would certainly recommend it to academics and nonacademics with an interest in biology or the philosophy of science. Some of the questions posed resonate outside the subject of this book, such as the issues of borders and identity, which are increasingly topical and urgent in today's society and would make for very interesting reading for those with a purely philosophical or social scientific interest in such subjects.

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