Thomas Pradeu. *The Limits of the Self: Immunology and Biological Identity*. Oxford University Press 2012. 320 pp. $69.00 USD (Hardcover ISBN 9780199775286).

The issue of identity is a metaphysical problem that cuts across different branches of philosophy. Biological identity is what makes a living entity both different from others and allows us to count it as one discrete and cohesive unit. According to T. Pradeu in *The Limits of the Self*, biological identity consists of that which makes a living entity both unique and individuated from others. He maintains that a non-evolutionary branch of biology, namely physiology, can inform questions of biological identity, especially identity in terms of individuality. The aim of this book is twofold: Pradeu not only proposes a more precise theory of immunology, but he also contributes to the philosophically-charged debate concerning biological individuals.

Pradeu argues that physiology is theoretically well-developed enough to provide a precise account of organismality. Specifically, the physiological field of immunology, or the mechanics of immunity, yields a clear definition of organismal individuality and identifies an organism as the most well-defined individual, rather than just one individual among many (264). Pradeu takes up David Hull's challenge to find a physiologically-based theory—one based on functional (or mechanistic) biology—to identify biological individuals (268). He maintains that immunologists respond to the issue of individuality by determining both the spatial boundaries drawn by the immune system and the maintenance of those boundaries over time (4, 8).

Through the majority of the book Pradeu develops his theory of immunology, which challenges F.M. Burnet's historically-established Self-Nonself Theory of how the immune system functions. Generally, immunity is considered to be an organism's capacity to react to an antigen—any substance that can trigger an immune response (17). Immunology is the study of all binding reactions between an organism's immune receptors and antigenic patterns consisting of ligands, which are molecules engaging in patterns of biochemical reactions (21). According to Pradeu, 'immunity is a ubiquitous phenomenon in nature' and he argues that a broad sense of immune functioning, i.e., the monitoring of spatial boundaries over time, occurs in both multicellular and unicellular life (22-44, 178ff, 263ff). For Burnet, however, an immune response is triggered by foreign or 'nonself' entities, which are genetically different from the organism and threaten its integrity (59). Under that classic framework only exogenous material is immunogenic, so the main individuating mechanism is 'difference that is genetic in origin' (61, 70). However, Burnet's immunological theory faces the following problems: First, an organism will tolerate exogenous and genetically different entities, such as symbiotic bacteria found in the human digestive system (see Chapter two 55ff; Chapter three 117ff). Second, often endogenous or non-foreign activity will challenge the integrity of an organism, such as cancer. Notably, Pradeu's discussion of cancer within the context of immunity is a valuable perspective for philosophers interested in disease and medicine, and is a recurring theme in the book (see Chapter three onwards from 89, 122-6, 170-2).

Pradeu proposes his own theory of immunology, the Continuity Theory, and aims to circumvent the problems that Burnet's theory could not overcome, such as responses to endogenous tumor antigens and tolerance of symbiotic bacteria (132). Pradeu keeps the criterion of immunogenicity, or the triggering of an immune response, as the precise marker of an organism's boundaries. However, immunogenicity is *not* due to the identification of foreign entities. Rather, it is due to strong modification of antigenic patterns, i.e., activity of molecules or ligands, that the organism's immune receptors interact with. In other words, there is an immune response when a

pattern is identified that differs strongly from those with which the immune system continuously interacts (131). Immunogenicity is caused by a strong discontinuous molecular difference, rather than exogenicity specifically (137). Therefore, both tolerance and rejection play a role in the maintenance of an organism's identity. Overall, Pradeu refines the Continuity Theory through his critique of Burnet's Self-Nonself Theory, as well as through a comparison with other immunological theories (Chapters three and five). Finally, Pradeu's theory of immunology provides an interesting perspective for the debate concerning evolutionary individuality, a debate engaged with philosophers such as P. Godfrey-Smith, J. Dupré and M. O'Malley, M. Ereshefsky and M. Pedroso, and E. Clarke. In Chapter six, Pradeu further develops how immunology delineates individuals in selection; an idea presented in his 2010 paper entitled 'What is an Organism? An Immunological Answer'.

The Theory of Evolution by Natural Selection (TENS) responds to the question of biological individuation by defining a hierarchy of individuals acted upon by selection. According to Pradeu, in that hierarchy organisms appear as only one individual among others, such as the gene, genome, cell, organism, group, or even species (9). Pradeu's Theory of Physiology by Immunology differs in that it identifies the organism as the most organized individual. The organism has physiological boundaries that are more differentiated, which render it sharply individuated compared to other entities (220). He maintains that immunology plays a privileged and significant role when addressing biological identity in terms of individuation (225-7). Immunogenicity is the criterion that monitors and maintains the spatio-temporal boundaries of individuals. It carves those boundaries with better precision than the vague functional integration criterion originally associated with physiology. Pradeu does not think of 'organism' and 'individual' as synonyms. However, he does think immunology yields a specific focus on organisms in the sense that one can evaluate another entity's degree of individuality by comparison to the organism as the most individuated case (229).

One point of controversy for philosophers may be how Pradeu conceives of biological individuals. He seems to think that there is only one way to individuate biological entities. For instance, he cites D. Hull's 1992 paper 'Individual' in which Hull states that non-evolutionary fields like physiology would be useful for determining biological individuals if they could offer theories (223). From this Hull infers that if individuation is always dependent on a theory, then the best way to individuate is with the best theory biology has, namely, TENS (234). However, in opposition to Pradeu it is reasonable to assume that there are not only evolutionary individuals, but also immunological individuals and perhaps even metabolic or reproductive individuals and so forth. These different types of biological individuality may overlap such that immunological individuation happens to pick out some individuals in selection. One may assume that Pradeu believes the physiological theory better delineates individuals in selection compared to TENS. On the contrary, however, I think Pradeu's message is that his physio-immunological criterion *coupled with* TENS is better at delineating individuality than TENS alone (256). He states that studying physiological processes is necessary to get a precise definition of evolutionary individuality, and calls for the acknowledgement of an explicit connection between immunology and evolutionary biology in terms of individuals (259-60, 268). This does not, however, amount to the claim that immunology is sufficient to determine evolutionary individuals. Regardless, it is questionable whether there is one true criterion of evolutionary individuation, and it is certainly very controversial whether there is one true criterion of biological individuation generally.

Pradeu's immunological criterion does appear to circumvent problems associated with integrated units comprised of parts which are genetically diverse. Criteria cited for evolutionary individuals often have issues accounting for symbiotic relationships that constitute a heterogeneous

unit. Pradeu can appeal to the active tolerance of an organism's immune system to address that concern, which captures the mosaic of heterogeneous individuals one finds in nature (258-9). Furthermore, debates concerning evolutionary individuality often address the emergence of new individuals through the process of de-Darwinization that P. Godfrey-Smith discusses in his book *Darwinian Populations and Natural Selection*. De-Darwinization is when a collection of entities transitions into an integrated individual unit. Pradeu is careful to point out that the immune system plays a major role in the control of emerging variants (261). This means that the immune system can prevent the emergence of lower level competition. An example of an immune dysfunction is the failure to prevent cancerous activity of cells in which the cells proliferate without dying. However, preventing the emergence of competition appears to be more akin to the *maintenance* of an individual rather than fostering conditions for the emergence of a *new* individual from a collection of entities. An immune system could prevent the breakdown of an individual, but may not necessarily create a new one. Nevertheless, Pradeu offers a new perspective of evolutionary individuality with insights that challenge the current discourse. Overall, I recommend this book to philosophers of biology and science who are interested in the notion of individuality, as well as to biologists concerned with the nature of individual organisms.

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