



Everything Flows: Towards a Processual Philosophy of Biology

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A Process Ontology for Macromolecular Biology

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Abstract and Keywords

This chapter argues (a) that macromolecules are fundamentally relational entities and (b) that only a process ontology can account for them. The basis for the argument is the ecological model proposed in 1981 by Charles Birch and John B. Cobb, which states that all entities, from atoms to populations, are ecosystems and hence fundamentally relational in character. The chapter first discusses how Birch and Cobb use the concept of internal relations to argue that ecosystems are processual in nature. It then shows that their account fails when it comes to macromolecules, as it does not offer an understanding of macromolecular behaviour in terms of internal relations. Following this, two case studies—symbiosis and enzyme function—are used for developing a fully relational account of molecular behaviour. This enables the expansion of Birch and Cobb's ecological model into a process framework that also applies to macromolecules.

Keywords: catalytic power, ecological model, process philosophy, protein biology, symbiotic systems

1. Introduction

Philosophers arguing for the need to adopt a process ontology often turn to the natural sciences to find support for their position. For instance, process philosophers have appealed to quantum physics because it 'puts money in the process philosopher's bank account' (Rescher 1996: 97), given its focus on fields and entangled states rather than on distinct entities. Some process philosophers have turned instead to the biological sciences, using in particular examples at

the organism or ecosystem level (see Birch and Cobb 1981; Dupré 2012; Henning 2013; and the other chapters in the present volume). A class of entities that has been almost completely ignored in these discussions, however, is that of macromolecules.¹ This is somewhat surprising, as macromolecules are arguably the entities that biologists have devoted most attention to in the last sixty to eighty years.

The dominant focus on examples at the quantum level and at the organism level raises several problems for current process frameworks. One is the issue of scope: it is not clear how much the existing accounts have to say about the macromolecular level. Due to their size—typical examples of macromolecules are proteins or DNA molecules—it is usually assumed that quantum effects (and hence quantum theory) can be safely ignored when dealing with macromolecules. So, even if there are good reasons to take quantum phenomena to be fundamentally processual, this does not mean that such arguments automatically apply to macromolecules. Moreover, although macromolecules constitute living systems, they are not themselves living, and consequently we cannot assume that what is said about the processual nature of organisms is automatically applicable to macromolecules.

And it is not just the scope of the existing accounts that is a potential issue for the process philosopher. A problem is also that the natural sciences usually represent molecules as well-defined, distinct entities that have inherent properties owing to their material constitution (i.e. their atomic microstructure). According to chemical **(p.304)** wisdom, molecules—including biochemicals such as DNA or proteins—look much more like substances than like processes.

What we are offered, then, by philosophers and by scientists alike, gives us little reason to assume that macromolecules are processual in nature. The goal of this chapter is to challenge this view and to argue (a) that macromolecules are fundamentally relational entities; and (b) that this relational nature of macromolecules is of a kind that only a process ontology can account for.

As the basis for my discussion, I will use the ecological worldview formulated thirty-five years ago by Charles Birch and John B. Cobb (1981). This ecological model represents an attempt to formulate a universally applicable process view of the world and states that everything, from atoms to populations, is an ecosystem and has to be treated as such. This means, according to Birch and Cobb, that all entities are fundamentally relational in character, which in turn means that only a process ontology can make sense of them. In section 2 I will introduce the ecological model and its assumptions in greater detail, highlighting in particular the importance of what Birch and Cobb call ‘internal relations’. This concept is used by them to characterize the specific type of relations we encounter in ecosystems (at all levels). This special form of relations is also the reason why ecosystems need to be understood as

fundamentally processual systems. In section 3 I will identify a key limitation of this account, namely its inability to provide an understanding of the capacities of molecules that builds on internal relations. I will show that this problem affects the macromolecular realm in particular and opens the door for a substance view of these crucial entities. The goal of the rest of the chapter will be to formulate a revised ecological account that can overcome this problem. To do so I will look at two case studies. In section 4 I will discuss the case of symbiotic systems, which show how we can develop a fully relational understanding of the capacities of biological entities. Key to this analysis will be the notion of ‘integrated capacities’, a term I will introduce to refer to capacities that depend on internal relations. In section 5 I will look at protein biology (and enzyme catalysis in particular) to show that this relational understanding of capacities also applies at the macromolecular level. With this revised understanding of capacities it will then be possible to formulate an extended ecological model that covers all entities, including macromolecules.

2. The Ecological Model of the World

The ecological worldview proposed by Birch and Cobb in their book *The Liberation of Life: From the Cell to the Community* is an attempt to formulate a general, process-based account of the world (Birch and Cobb 1981). The model is based on two key claims: (1) everything—from atoms to organisms to populations—is an ecosystem, as opposed to some sort of machine or mechanism (ibid., 89);² and (2) an ecosystem model of the world goes hand in hand with a process ontology, since ecosystems are **(p.305)** fundamentally relational in nature.³ In what follows I will look at these two claims in more detail.

2.1. Ecosystems, machines, and the environment

The reason for Birch and Cobb’s (1981) first claim is mostly empirical: they argue that, if we look at what the sciences are telling us about the world, we see that a machine view simply does not fit in with how the world works (or is assumed to work).⁴ In the machine/mechanistic framework, entities are seen as distinct beings disconnected from each other, much like separated boxes. What allows each entity to behave the way it does is its internal structure, not the relations it has to its environment. Apart from providing some essential ‘enabling’ factors (such as a source of power) the environment has no significant bearing on the functioning of the machine parts or on the machine itself.

The ecological model paints a very different picture of the world, as it does not treat it as a set of disconnected boxes. Rather, entities are seen as interconnected complexes that behave the way they do because of the relations they have to other entities and/or processes in their environment (ibid., 83). In this view, the environment always needs to be taken into account when analysing the workings of entities, as it is (part of) what determines how entities behave.

Birch and Cobb claim that the ecological view is actually what the sciences present us with and what practising scientists have long adopted (even those who call themselves mechanists).⁵ Especially in studies of animal behaviour, according to Birch and Cobb, researchers have always been forced to acknowledge the importance of context, as these studies have invariably shown that the behaviour of animals is fundamentally altered by changes in the environment of the animal (*ibid.*, 80).

2.2. Internal versus external relations

Adopting a mechanistic view does not mean, of course, that relations are neglected or disposed of. We can easily see this when we look at the importance of factoring in context sensitivity and context dependence when explaining or predicting the behaviour of machines or machine parts. Context dependence means that external relations ('inputs') are required for the correct functioning of the parts or of the machine. A cogwheel, for instance, turns because of the relations it has to other components of the machine it is a part of; what the cogwheel does depends on the relations it has to other entities or processes in its environment. This might seem like a trivial point, **(p.306)** but it is important as it shows that factoring in relations is at the very core of the machine view.

Context sensitivity also has a role to play in a machine view, as even a simple part such as a steel rod is a context-sensitive entity that will, for instance, expand or contract in response to changes in the temperature of its environment. Such a change in length can have a significant effect on the functioning of a machine, which means that context sensitivity becomes a crucial aspect that needs to be accounted for when analysing or predicting the workings of a machine.

The reason why context sensitivity is compatible with a machine view is that it can be treated as an intrinsic feature of an entity. A steel rod might expand or contract depending on changes in its environment, but the way it responds to such changes is usually seen as an intrinsic feature or capacity of the particular type of steel the rod is made out of. The (potential) behaviour of the rod is seen as being determined by its material composition and structure rather than by its relations to other processes or entities. Other rods composed of different materials will display their own 'characteristic' capacity to expand or contract, as their microstructure is different. When we assume such context-insensitive context sensitivity, we are still operating within the disconnected boxes model that Birch and Cobb identify as one of the hallmarks of the machine view. Simply developing a relational account that acknowledges the importance of relations is therefore not enough to get the machine view into trouble.

Birch and Cobb are well aware of this, which is why they introduce a distinction between *internal* and *external* relations to deal with it. With this distinction they want to emphasize that what matters is not whether there *are* relations, but

what role they play in the system of interest. In a mechanical system, Birch and Cobb maintain, relations are merely external, which means that the nature of an entity is not affected by the relations it has with other things or processes. The cogwheel or the steel rod are not affected in their nature by their (external) relations or by the change (turning, expanding, contracting) they undergo. The way they react to changes in their context is set by their material constitution.

In an ecological system, what a thing is depends on the relations it has; this means that there are no 'merely external' relations. The relations always have a constitutive role to play and hence are to be treated as internal:

The ecological model proposes that...the constituent elements of the structure [i.e. an entity of interest] operate in patterns of interconnectedness which are not mechanical. Each element behaves as it does because of the relations it has to other elements in the whole, and these relations are not well understood in terms of the laws of mechanics. The true character of these relations is discussed in the following...as 'internal' relations.

(Birch and Cobb 1981: 83)

2.3. Substance versus process

The contrast between the two different types of relations also brings us to Birch and Cobb's second claim, namely that there needs to be a switch from a substance to a process ontology if we are to switch from a machine to an ecological model. According to Birch and Cobb, a substance is exactly the type of entity that a machine view of the world presupposes, given that a substance is something that is not affected (**p.307**) in its nature by the relations it has. Relations are always external to a substance.⁶ But, since a machine/mechanism view is not supported by what the natural sciences are telling us about the world, the substance ontology that underlies it has to be replaced by something that fits the ecosystem structure of the world.

The replacement Birch and Cobb have in mind is what they call an event ontology (see n. 3). According to this account, the behaviour of a system has to be explained by reference to events and not underlying substances. Importantly, events are 'constituted by their interconnectedness with other events' (Birch and Cobb 1981: 88), which means that relations are constitutive of (and, in the authors' terminology, internal to) events. This also means that there is no event that simply preexists and then relates to other things; in abstraction from its relation to the environment, the event itself is nothing (*ibid.*, 87).

The switch from a substance to an event ontology also includes a reversal of the explanatory aims: whereas a substance ontologist aims to explain events that happen in the world in terms of substances, someone adopting an ecological worldview or an event ontology will aim to explain how persisting objects come

about through an interconnection between events (ibid., 86). Importantly, the focus on events does not mean that there is no place for stable entities in an ecological model of the world. Events are simply seen as the *primary* elements of the world and stable entities are treated as ‘enduring patterns among changing events’ (ibid.: 95).

What is interesting about the account Birch and Cobb develop (and where, I think, it goes beyond the work of Whitehead it builds on) is the notion of ‘ecological system’ that it brings into the discussion. This concept gives us a different and powerful framework within which to think about the specific relational—and hence processual—character of entities at different levels of organization. The ecological model, in principle at least, offers a way of formulating a unified process framework that might apply to organisms and quantum systems as well as to the entities in between: macromolecules. But, as I will discuss in the next section, this unification is not without its difficulties.

3. Problems with the Ecological Model

It is clear from what we have discussed so far that the ecological account is meant to apply to all levels of entities, from single atoms to populations of organisms. However, beyond some general statements about atoms and molecules being ecosystems, Birch and Cobb offer little evidence to substantiate their radical claims about the nature of molecules. The problem is not that they do not discuss examples taken at the molecular level. It is rather that the examples they give do not seem to support their claims, as they do not establish how molecules are defined by internal rather than external relations.

We see this problem when we consider their discussion of DNA and its workings. As in the case of animal behaviour mentioned earlier, Birch and Cobb point out that empirical work on DNA has shown that its behaviour is highly context-sensitive and **(p.308)** context-dependent; the way DNA behaves is always affected by, and depends on, the particular environment it finds itself in.

The problem is that their discussion of DNA behaviour does not give us any reason to go beyond the type of context sensitivity that depends merely on external relations, which we encounter in the case of machines. How close their description of DNA is to the machine view becomes particularly clear when they say: ‘The DNA in the nucleus of the fertilised egg contains all the instructions necessary to make all the different proteins and all the different sorts of structures in all the different sorts of cells in the body...But not all the instructions are needed by every cell’ (Birch and Cobb 1981: 81). Applying this view of DNA to the example of gene regulation in bacteria they go on to state that ‘in their normal life in our intestines...bacteria must be ready to change their enzymes quickly to suit the sort of sugar we send down to them. They are selecting just one from the several that their DNA allows them to produce’ (ibid., 81).

What stands out here is that the DNA molecule is portrayed by Birch and Cobb as having an intrinsic capacity to code for different products (proteins and other 'structures'). This capacity does not come about through relations but is given by the structure of the DNA, which means that it is contained within the DNA itself. It is only the *realization* of these capacities that depends on the interaction of DNA with specific enabling factors in its environment; what part of the DNA becomes activated in what way and at what time depends on contextual elements such as transcription factors or methylation patterns. But the set of options is restricted and, most importantly, defined by the intrinsic properties of DNA. The relations with the environment do not change what the DNA is and what capacities it has.

Such a view clearly still adheres to the machine view that Birch and Cobb want to avoid, as it operates with a picture of DNA as an entity for which relations are merely external; the context is what selects externally from a potential that is defined by the structure of the DNA itself. The more radical claims Birch and Cobb make about the fundamentally relational nature of molecules are therefore not supported by their own descriptions of the functioning of DNA.

The DNA example shows that the ecological account potentially faces a serious challenge when it comes to macromolecules, as its current formulation does not offer a fully relational understanding of their capacities. By describing macromolecules such as DNA as entities that ultimately don't depend on internal relations, Birch and Cobb leave the door open for a machine interpretation of this crucial class of entities. The problem is that the ecological model in its current formulation is missing a fully relational understanding of capacities. In the next section I will address this issue and claim that recent research on symbiotic systems can show us a way to such a relational account. To characterize what is special about this alternative view of capacities, I will introduce a distinction between 'component' and 'integrated' capacities.

4. Symbiosis and the Importance of Integrated Capacities

In recent decades, research in biology and ecology has greatly advanced our knowledge of how complex organisms and ecosystems persist and reproduce themselves. **(p.309)** This research has also shown that symbiotic life forms are the rule rather than the exception in the biological realm.⁷

Symbiotic systems are systems in which (in the simplest case) two organisms form a tight relationship with each other from which either one side or, in the case of mutualism, both sides benefit. Often the organisms involved depend on the symbiotic relationship for their survival, in which case scientists talk of obligate symbionts. In this section I will discuss the case of termite colonies in order to show how symbiotic systems help us gain a more relational understanding of capacities. In section 5 I will then show how this alternative understanding of capacities can also be applied to macromolecules.

4.1. Termites and their capacity to survive and reproduce

My discussion of symbiosis will focus on the work of J. Scott Turner, who studies termites of the genus *Macrotermes*, which live in southern Africa.⁸ These termites form large structures, within which they cultivate a specific type of fungus, which can digest the cellulose in wood or grass—the termites' main source of food.

A prominent feature of these structures is the tall mounds that mark the location of a termite colony. The mounds can grow up to thirty feet in height and contain an intricate internal structure consisting of a central 'chimney' connected to a network of passages and thin-walled tunnels. Interestingly, these mounds do not serve as housing for the termites, which live in a spherical nest below the mound. Turner's (2000) work suggests that the mounds rather serve as something like a lung, helping to maintain specific atmospheric conditions inside the colony.

These specific atmospheric conditions are required to guarantee the survival of the colony. The reason for this requirement lies in the demands of the fungi that form part of the colony: to work at the optimal rate, they require sufficient oxygen and the right temperature and humidity. And it is here that the mound and its complex network of chimneys and tunnels come into play: the mound, Turner proposes, harvests air currents on the surface and channels it into the mound, allowing a tightly regulated turnover of the air within the termite colony and thereby creating (part of) the conditions needed for its functioning. Turner found that the oxygen concentration within the nest is kept at 17 per cent (which is 2 per cent lower than the atmospheric concentration of oxygen) and humidity is kept at 70 per cent (as compared to an average of 20 per cent on the outside).

The termites constantly rework the structure of the mound, to make sure that these conditions are maintained. This makes the mound, as Turner puts it, a process rather than a static object. Interestingly, even though the termites are a key force that shapes the mound and the nest, Turner found that this shaping takes place also because of the activity of the fungus. This is because the growth of the fungus can cause it to break through the surface of the mound, thereby creating leaks that the termites then fill in and repair (Turner 2005). This 'dance of agency', to use Andrew Pickering's term (Pickering 1995), turns out to be a key force in the shaping of the mound and **(p.310)** the nest: the formative power here is a meshwork of activities rather than the activity of just one particular entity (e.g. the termites).

The termites' case nicely illustrates that (as in other cases of symbiosis) all the elements of the system have to work together to bring about a colony that can survive and reproduce. As Turner puts it, '[t]he termite colony—insects, fungus, mound, and nest—becomes like any other body that is composed of functionally

different parts working in concert and is ultimately capable of reproducing itself. Taken as a whole, the colony is an extended organism' (Turner 2002: 66).⁹

4.2. Process and individuality

The termites' case illustrates an important and more general challenge, which has gained significant attention in philosophy of biology in recent years: as even the soil-based mound has to be seen as an integral part of the superorganism, our traditional understanding of what a biological individual is becomes seriously undermined by such life forms (Clarke 2010; Gilbert et al. 2012; Bouchard and Huneman 2013; Ereshefsky and Pedroso 2013; Guay and Pradeu 2015). The problem of biological individuality is brought up not only by the termites' case but by all forms of symbiosis and has also been used to argue for the need to adopt a process ontology (see Dupré 2012, Henning 2013, and—again—chapters 1, 5, 9, and 10 here).

Brian Henning in particular argues that through Turner's work on termites we come to realize that 'a single termite is unintelligible apart from the collective organism of which it is a member' (Henning 2013: 240). He then adds:

Individuals normally have clearly defined boundaries, a membrane that demarcates where they begin and end. Here we find that, as a single superorganism, the termite colony is extended in space and time, without clearly defined boundaries or a skin to define where the environment stops and the superorganism begins. Normally we would say that a single insect crawling on the ground is a proper individual. However, Turner's research shows that a single termite is no more an individual than a single cell in a petri dish solution.

(Ibid., 241)

Henning claims that this blurring of boundaries challenges the substance-based metaphysics our traditional notions of individuality rely on; in other words a process ontology (à la Whitehead, in this case) is required to make sense of the ontological status of what Henning calls 'collective individuals'.

In his discussion Henning emphasizes the absence of sharp boundaries between the superorganism and the environment. But it is not immediately obvious in what sense boundaries become blurred here, as he is clearly able to talk about the individual termites, which he identifies as distinct, well-defined entities and which Turner tracks and studies without any (conceptual) problems. Turner is also clear about what distinct entities belong to the colony (mound, termites, fungus, etc.). So certainly not all dividing lines we are used to drawing around entities are undermined by symbiosis. But what does Henning mean, then, when he claims that the single **(p.311)** termite is 'unintelligible' to us apart from the

larger system and that we need a process ontology in order to be able to account for what makes a ‘proper’ individual?

4.3. Distributed capacities

What I think is crucial here—and this is something that Henning (2013) does not directly emphasize—is the strong focus on capacities. This observation is not limited to Henning’s paper but applies more generally to discussions of symbiotic systems. If we look at the previous example, we see that what is not intelligible in the case of the isolated termite is how some of its capacities come about. The discussion shows that the boundaries that are being brought down by the termite case are not the physical boundaries around the different entities, but the boundaries we draw around the autonomous being, the thing that ‘does’ something. The significance of symbiosis examples in general is in the realization they give us that the entities we used to refer to as single living things (for instance termites moving around, eating, and digesting food) turn out to be less autonomous than we might have thought them to be: in order to function the way they do, they need the other elements of the symbiotic system. This is the sense in which they are not ‘proper’ individuals anymore.

What is shifting in our understanding of the termite (or other organisms, for that matter) is the *attribution of the power to do things*.¹⁰ We are moving from considering only one thing as the carrier of a certain power to considering a network of entities as the legitimate carrier of that power: it is not just the termite that shapes the mound and has the power to digest, reproduce and survive, but a system of interconnected entities that has to be treated as the centre or origin of these capacities or powers. What changes is our understanding of where to place capacities we normally ascribe to entities demarcated through clearly distinct boundaries (e.g. a membrane or some sort of skin).

4.4. The ecology of powers

The symbiosis example shows that collaboration is at the core of what defines living systems: different entities have to work together to achieve a particular goal, such as survival or reproduction (Dupré and O’Malley 2009). But why should the importance of working together mean that we have to abandon a substance ontology and adopt a process view instead? After all, the idea of collaboration is, by itself, fully compatible with a substance-based understanding of the world. Quite trivially, the capacity of a machine—for example, the capacity of a car to turn left or right—usually comes about because several parts of that machine (with their individual properties and capacities) work together. In a machine view, it is assumed that each of the parts involved has its own set of subcapacities, which contribute to the overall system capacity, and that the parts have these subcapacities because of their specific composition (and not because of their relations to the other parts of the machine).

If symbiosis could be reduced to such an understanding of collaboration, then the termite example would not force us to move away from a machine view. And it is **(p.312)** tempting to treat the termite system in this way, for instance when considering its capacity to digest grass or wood. At first sight this capacity seems to be the outcome of two distinct parts working together, namely the termite that delivers wood or grass to the nest and the fungus cells that digest the cellulose contained in this material, breaking it into single sugar molecules (which in turn serve as food for the termites).

But the working together of the different parts in symbiosis is not the same as the working together of the parts in a machine, as we cannot simply take the termite as a moving (and mowing) device that collects grass or wood and the fungus as a digestive apparatus, then plug the two together, each coming with its own independent and preexisting set of capacities. What is crucial about the powers we ascribe to the termite colony and its parts is rather the constant interaction between (the activities of) the entities of the larger system. All these activities and interactions are interconnected and interdependent in such a way that, if they were to stop, then the key properties of the system and of what we describe as its parts would disappear.

This interdependence becomes clear if we consider how the different parts come to have the subcapacities we usually ascribe to them. If we, for instance, take a closer look at the ability of fungus cells to digest cellulose, we quickly learn that the actual degradation of cellulose molecules is performed by enzymes that are produced by the fungus cells (see Baldrian and Valaskova 2008 for an overview). We also know, from basic cell biology, that the fungus cells need specific subcellular compartments (e.g. the so-called 'endoplasmic reticulum') to function properly. But, to be able to form the different intracellular structures and have them work as they should, the fungus cell needs particular conditions, including a specific temperature or oxygen concentration. Importantly, as the work of Turner shows (section 4.1), these parameters are not simply inherent properties of the nest or the soil but themselves the results of ongoing processes such as the movement of air through the tunnels that are created and constantly maintained by the termites, or the digesting activity of the fungus cells. The capacities we find in complex biological systems are therefore not simply preexisting features of its parts that merely need to be activated by (external) relations but features that only come about through what Birch and Cobb call internal relations. To find terminology that allows us to describe this specific form of relational capacities, I will turn now to the work of William Bechtel and Robert Richardson.

4.5. Component versus integrated capacities

In their book *Discovering Complexity*, Bechtel and Richardson develop a framework that can be used to analyse different types of complex systems (Bechtel and Richardson 2010). This framework, I think, can also be helpful for

the present discussion about complex capacities. Following the work of William Wimsatt and also Herbert Simon, Bechtel and Richardson distinguish between aggregative systems and composite systems, the latter being further subdivided into *component* and *integrated* systems. Aggregative systems are those in which (a) each component has an intrinsic function or behaviour; and (b) the organization of the components does not affect their behaviour. As a consequence, the overall behaviour of the system is a function of component behaviour and does not depend on the organization of the parts (ibid., 25).

(p.313) In composite systems the organization of the system (and hence the environment of the different parts) starts to play a role in the behaviour of the system and its parts. In a *component* system the behaviour of each component is still determined by its intrinsic features, but the organization of the system affects the behaviour of the whole and its parts (this is basically what Birch and Cobb call a machine or a mechanism). In an *integrated* system the behaviour of each component is no longer intrinsically determined, as the organization of the whole becomes a key determining factor of each component's capacity to act (this corresponds to what Birch and Cobb call an ecosystem).

This distinction between component and integrated systems can also be useful for the discussion about capacities and the different forms of collaboration we encounter in the machine and ecosystem cases. In a substance ontology/machine view, the capacities of the individual parts are treated as inherent in the self-contained, distinct entities that compose the system. These capacities are intrinsic and simply need an external 'trigger' or stimulus and a 'nurturing' or 'enabling' environment. When working together, they might respond to inputs from the other elements of the system but their way of reacting—their repertoire of possible behaviours—is intrinsically determined. These are what I will call 'component capacities'. In the case of symbiotic systems, the property of having a power or capacity is not some intrinsic feature of preexisting entities, but a relational feature that comes about within the system of interest through the intersection of different processes (or, in the terminology of Birch and Cobb, events). The context becomes a constitutive factor for these capacities, which is why I will refer to them as 'integrated capacities'.

4.6. Integrated capacities at all levels?

As we discussed in section 2, the Achilles heel of the ecological account is that it does not offer a fully relational understanding of the behaviour of macromolecules. Interestingly, the symbiosis example offers an understanding of capacities as relational properties and can therefore provide an important extension of the ecological view. The question is whether this relational understanding of capacities can be extended to the macromolecular level and therefore lead us to a process framework that applies to all levels of entities.

At first sight such an extension seems problematic, as macromolecules don't seem to be prone to individuality issues, like symbiotic systems. There are no 'supermolecules' for which the boundary between entity and environment becomes blurred, as it was the case for the termite colony; the ascription of capacities simply does not seem to be an issue at the molecular level. This is illustrated not only by the case of DNA, discussed in section 3, but also by other macromolecules, for instance proteins. In the molecular life sciences proteins are usually treated as 'molecular machines'. The capacities of these machines do not depend on relations, but on being the right kind of entity, that is, a molecule with a particular structure (a three-dimensional fold, in the case of proteins) and composition (the amino acid sequence of a protein). The capacities of proteins are therefore treated as component, and not as integrated, capacities. However, as I will show in the next section, this picture of macromolecules as carriers of component capacities quickly falls apart if we look closer at how these entities actually work. Capacities at the macromolecular level (**p.314**) ultimately turn out to be as integrated as those ascribed to symbiotic systems, at least if we follow how scientists themselves try to make sense of the powers of proteins.

5. Proteins, Structure, and Capacities

Proteins are linear polymers of amino acids, linked to one another via peptide bonds (which is why they are often called 'polypeptides'). Proteins are often portrayed as the 'doers' or the 'workhorses' of the cell, a characterization that is mostly reserved for enzymes—the proteins that have the ability to catalyse chemical reactions. An example of such workhorses are the kinases, a class of enzymes that have the ability to mediate phosphorylation, that is, the transfer of a phosphate group from a donor to a target molecule (usually another protein). That the kinases are presented as the carriers of specific intrinsic powers can be seen in any review or research article that talks about them. If we pick a random example of a paper that has the word 'kinase' in its title (here I chose Ubersax and Ferrell 2007), we quickly find claims such as these: 'Despite sharing a common fold, kinases bind to and phosphorylate different protein substrates'; 'Non-systematic studies and biochemical lore suggest that kinases vary greatly in the number of these sites that they phosphorylate.'¹¹ Clearly kinases are presented in these passages as the carriers of the capacity or power to phosphorylate target molecules. Importantly, this capacity is not treated as a relational feature of a larger system but as an inherent (and defining) property of the kinase itself. This means that it is treated as a component rather than as an integrated capacity.

5.1. From structure to power?

But how do enzymes like kinases obtain their power? Enzymes are catalysts that function by lowering the activation energy of a chemical reaction. According to the transition-state theory of chemical reactions, each chemical reaction has to go through a transition state, which represents the maximum energy point along the reaction pathway. The reason for this is that a high-energy intermediate

between the substrate and the product of the reaction is being formed in the transition state. The energy required to reach this intermediate is called the activation energy of the reaction.

The role of the catalyst is to lower the energy required to reach the transition state, in other words, to lower the activation energy of the reaction. By doing so, the catalyst allows the reaction to take place at a higher rate at a given temperature, since more substrate molecules in the mixture will have the required energy to overcome the activation barrier.

How do enzymes achieve this feat? Explanations of how proteins function are regularly given using what some refer to as the sequence–structure–function (SSF) paradigm (see e.g. Wright and Dyson 1999 or Redfern et al. 2008). The SSF has been central to protein biology, roughly, for the past hundred years; it postulates that the **(p.315)** function of a protein is determined by its three-dimensional structure, which in turn is determined by its unique amino acid composition and sequence (i.e. by its atomic composition and organization). The interactions between the atoms of these different amino acids allow the polypeptide to take on a specific three-dimensional conformation. The interactions between amino acid residues (both backbone and side chain atoms) can range from hydrophobic interactions to electrostatic or covalent bonds. According to the SSF paradigm, it is the composition and the sequence of the protein that determines the structure it can obtain. This structure then determines what the protein can do, that is, what specific powers it has. The SSF paradigm therefore presents proteins as distinct entities that possess specific capacities due to their inherent properties—a picture that is perfectly in line with a substance-based understanding of molecules.

What is special about the structure of enzymes is that they possess a so-called ‘active site’ in which the side chains of specific amino acid residues are spatially arranged in a particular way. This specific arrangement of the amino acids forms a chemical environment that allows the enzyme to function as a catalyst, as it enables it to bind to the high-energy intermediate and thereby stabilize it (or so the SSF paradigm would imply). This stabilization indicates that the energy required to reach the transition state of the reaction is lowered, which means that the rate at which the reaction proceeds at a given temperature is increased owing to the presence of the enzyme.

This explanation of enzyme function using the SSF paradigm shows us an important qualification of the picture of the enzyme as a ‘doer’ that we encountered earlier and that is so prevalent in the ways scientists talk and write about molecules: if we look at the story of enzyme action in more detail, we see that what the enzyme does is to provide a particular chemical environment, a surface that allows different molecules to interact in specific ways (the active site). These interactions ultimately are what allows the system as a whole to

undergo a transformation along a different reaction pathway, which means a path with a lower activation energy. Enzyme catalysis is a much more collaborative enterprise than one might think, judging by how scientists usually talk about enzymes. And the picture of the enzyme as some sort of machine or workhorse that actively phosphorylates a target is clearly a highly metaphorical way of portraying what is going on.

But, as we have seen earlier, the mere fact that collaboration is important does not mean that we have a system that operates with integrated rather than component capacities. If we want to argue that a machine view could not account for the functioning of enzymes, we need to show that, also in this case, we have integrated capacities at work. To do so I will turn to the work of the chemist and process philosopher Ross Stein and to his discussion of recent developments in enzyme research.

5.2. More than just collaboration

Stein's work is interesting for our current discussion because he follows Birch and Cobb in claiming that molecules (and enzymes in particular) are ecosystems. To support this claim, Stein considers new models of enzyme function developed in enzymology. What is special about these models is that they no longer portray **(p.316)** three-dimensional structure as some sort of stiff scaffold, but rather as a dynamic feature of the protein. A protein, according to these models, is better represented by an ensemble of similar but different structures rather than by one fixed structure. And, importantly, the protein is assumed to constantly cycle through the conformations that form its ensemble.¹²

What makes this new view of enzymes particularly interesting is that this activity of cycling through different conformations is taken to be crucial for the functioning of the enzymes. The idea is that enzymes have the power to stabilize the high-energy transition state of a specific reaction *because* of the dynamics of their structure. And the enzyme can only cycle through its different states because it is coupled to the environment, that is, to the thermal motion of the bulk water that surrounds it. It is this complex interaction with the surrounding water that ultimately shapes the way the enzyme behaves and that gives rise to the power to catalyse a chemical reaction.

This provides a crucial reinterpretation of the way power is attributed to an enzyme: the three-dimensional structure, the only element deemed relevant in the SSF paradigm, is no longer enough to bring about function. What matters for the power of the enzyme to catalyse a reaction is rather the constant change in its polypeptide. Importantly, this change only comes about because of the enzyme's interaction with the surrounding water.

To Stein, this is the key change, as the two 'parts'—the enzyme and the surrounding bulk of water—are now treated as a unit (Stein 2004: 15). And it is

out of this unit that the capacity to catalyse a chemical reaction arises. As he puts it:

In the end, we will not be able to locate the origins of the catalytic power of an enzyme in a certain 3-dimensional arrangement of active site residues nor in a certain fold of the protein; rather, enzymatic catalysis will have to be analyzed as structurally specific substrates bound to an active site of definite chemical potential embedded in a dynamic protein matrix that is in thermal exchange with the aqueous environment of bulk solvent. This holistic description of enzyme catalysis can be solidly grounded in the metaphysical foundation of Strong Chemical Processism.

(Ibid., 15)

Stein's discussion of recent work in enzymology illustrates how the structure of the protein is no longer seen by scientists as the factor that brings about the capacity of an enzyme to catalyse a chemical reaction. It is also no longer the case that the environment is simply treated as the provider of an energy input that then activates the capacity of the enzyme. The interaction between water and enzyme (neither of which is now demoted to the role of mere external environment) is what brings about the capacity to catalyse the reaction. The boundaries between the enzyme and its environment therefore become blurred, much as in the case of the symbiotic system discussed in section 4. And what we end up with—once we focus on this question of where the capacity resides and how it comes about—is a picture of integrated rather than component capacities of proteins.

(p.317) 5.3. *Towards a general process account for macromolecular biology*

Stein's approach is of course not without its problems, especially in light of its explicit goal to provide a general process framework that applies to all molecules (and other entities). One issue is that the model Stein discusses might not apply to all enzymes, as there could well be some that do not depend on the environment in the same way his chosen examples do. Furthermore, even if the model applied to all enzymes, it is not clear in what sense proteins that are not enzymes could be equated with ecosystems, as they might have very different modes of functioning.

There are at least two ways to answer such worries about the scope of Stein's account. First, it is crucial, I think, to put his discussion of enzymes into the context of current developments in protein biology more generally, in particular the discovery of intrinsically disordered proteins mentioned earlier (see n. 12). The IDP case convincingly shows that the dynamic nature of the polypeptide has a crucial role to play in the functioning of many more proteins than just enzymes.¹³ The prevalence and importance of IDPs for the functioning of the cell undermines the strict link between structure and function that the SSF

paradigm postulates, which has important consequences for our understanding of the nature of proteins more generally.

But there is also a second way of making Stein's discussion broader; and this is by questioning the first part of the SSF paradigm, that is, the link between the sequence (microstructure) of a protein and its three-dimensional structure. Stein focuses his discussion of enzymes on the second part of the paradigm, the link between the structure and function of proteins. But the question of how proteins obtain their powers also comes up, of course, when we consider the first part of the SSF paradigm, which states that the sequence of the protein is what defines the structure(s) it can adopt. As in the case of catalytic power, the capacity to adopt a particular fold is treated as an intrinsic feature of the protein (if we follow the SSF paradigm) that only depends on (external) relations.

Interestingly, once we dig deeper into the question of how a protein can adopt a particular three-dimensional conformation (or an ensemble of conformations), we are immediately led to talk about forces. As briefly mentioned in section 5.1, different physical forces are at work when the crucial interactions of a particular conformation of a molecule are formed. One such force that is crucial for the fold of a protein (but also for the double-helix structure of DNA) is the hydrophobic force, a sort of repulsion from water felt by hydrophobic (i.e. apolar) molecules.¹⁴ All structured proteins have a hydrophobic core in which apolar amino acids are 'buried', that is, kept away from the protein's aqueous environment. The formation of this hydrophobic core is an important step in the folding process and is also what to a large extent explains the relative stability of folded proteins. A similar process is at work in DNA, where the stability of the double helix depends not only on hydrogen bonds (**p.318**) formed between matching base pairs but also on hydrophobic interactions between the stacked nucleotides (Yakovchuk et al. 2006).¹⁵

The hydrophobic force is interesting for our current discussion because it is not something a single molecule simply possesses, given its intrinsic properties. It is rather a phenomenon that comes about through the interaction of a larger system of (polar and apolar) molecules. It is also not just the mere existence of polar and apolar entities that gives rise to the hydrophobic force. The force only comes about in a context of constant interaction and repulsion; it is a force born out of becoming, and not out of simple being. The structure that the protein (or any molecule, for that matter) adopts is therefore the outcome of a complex process, which takes place within a larger dynamic system. Within this system it is not clearly defined what should be seen as 'internal' and what as 'external', since the boundaries between the entity of interest and its environment are blurred. The capacity to adopt a particular fold is therefore not something that the protein simply possesses and that is then triggered or activated by some external input from the environment but it is, like the catalytic power Stein

discusses, or like the capacities of a termite colony, an integrated capacity that emerges from within an integrated whole.

6. Conclusions

The goal of this chapter was to show that macromolecules such as proteins or DNA molecules are ecosystems in the sense of Birch and Cobb, in other words, that they are relational entities that can only be fully accounted for by a process ontology. As I argued in section 3, the original ecological model suffers from the problem that it does not offer a fully relational understanding of the capacities of macromolecules. I used the example of termite colonies to develop a relational understanding of capacities ('integrated capacities') and I then argued that such integrated capacities are also what defines the behaviour of molecular systems, be that catalytic activity or the activity of folding into a particular three-dimensional structure. With this fully relational understanding of macromolecules it becomes clear that they, too, are ecosystems, as Birch and Cobb postulated. Being ecosystems means that they are fundamentally processual entities, which in turn means that the ecological account can now fill the gap between the quantum and the organism level and offer a general process framework that also includes macromolecules.

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Notes:

(¹) A rare exception is Ross Stein (2004, 2006), whose work I examine in section 5.

(²) Birch and Cobb use the terms 'machine' and 'mechanism' interchangeably. Also, when talking about something's being an ecosystem, Birch and Cobb not only mean that everything has to be treated as if it were an ecosystem but that all entities *are* ecosystems.

(³) Birch and Cobb consistently talk of an 'event ontology' rather than a 'process ontology' (in fact the word 'process' does not even appear in the index of their book). However, this does not mean that the term 'process ontology' is out of place to describe their position. Not only are the two widely seen as process philosophers (or, maybe better, as a 'process biologist' in Birch's case), but they also state that their ecological model is in principle the same as Whitehead's philosophy of organism (i.e. his process ontology; see Birch and Cobb 1981: 8).

(⁴) For an extended discussion of the problems with the machine view in relation to the project of developing a process ontology for biology, see chapter 7.

(⁵) Stein (2004: 10) makes a similar claim about the situation in the chemical sciences.

⁽⁶⁾ Birch and Cobb call a machine/mechanistic model a ‘natural expression of substance-thinking’ (Birch and Cobb 1981: 85). A similar claim is advanced in chapter 1 of this volume.

⁽⁷⁾ The philosophical significance of symbiosis is also examined in chapters 1, 5, 9, and 10.

⁽⁸⁾ For an overview, see Turner 2002, but also Henning 2013, which uses the termite case to argue for the need for a process ontology. I discuss Henning’s work in section 4.2.

⁽⁹⁾ For more on the heteronomy of organisms and other biological entities, see Dupré and O’Malley 2009.

⁽¹⁰⁾ In what follows I will use the terms ‘power’ and ‘capacity’ interchangeably. Note that my use of the term ‘power’ does not necessarily correspond to the more technical meaning this concept often has in metaphysics (see e.g. chapter 3 in this volume).

⁽¹¹⁾ We also find similar statements in textbooks, for instance the key textbook *Molecular Biology of the Cell*, where the authors state: ‘The protein kinases that phosphorylate proteins in eukaryotic cells belong to a very large family of enzymes, which share a catalytic (kinase) sequence of about 290 amino acids’ (Alberts et al. 2008: 176).

⁽¹²⁾ This view of proteins is in line with a more general development in protein biology that acknowledges the fundamentally dynamic nature of proteins. In particular, the discovery of what is now called ‘intrinsically disordered proteins’ (IDPs) has provoked a change in our understanding of proteins (for a general overview, see Dunker et al. 2001).

⁽¹³⁾ It is estimated that 30–50 per cent of all proteins are IDPs (Dunker et al. 2001). Note that most of the known IDPs are not enzymes.

⁽¹⁴⁾ In the case of proteins, these are mostly the apolar side chains of specific amino acids such as alanine or leucine. In the case of DNA, these are apolar parts of the nucleotides that form the DNA.

⁽¹⁵⁾ DNA is in general a much more dynamic entity than is often assumed. The depiction of DNA as some sort of stable double helix that can at most wind itself around some histones ignores such interesting features as ‘DNA breathing’, the constant opening and closing of the double helix that is—again—crucial for its proper functioning (see von Hippel et al. 2013; Fei and Ha 2013).

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