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Reviewer's report on the PhD of Mr Adrian Stencel

Title of the Doctoral Thesis: "A reconceptualization of the basis of population biology: The case of animal interactions with microorganisms."

This thesis takes the form of the following three papers:

1. Stencel A. and Włoch-Salamon D. 2018: Some Theoretical Insight into Hologenome Theory of Evolution and the Role of Microbes in Speciation. Theory in Biosciences, 137: 197–206

2. Stencel A. and Proszewska A. 2018: How Research on Microbiomes Is Changing Biology: A Discussion on the Concept of the Organism. Foundations of Science, 23: 603–620.

3. Stencel A**.** 2016: The Relativity of Darwinian Populations and the Ecology of Endosymbiosis. Biology & Philosophy 31 (5): 619–637.

The Board of the Field "Philosophy" at the Jagiellonian University in Krakow, Poland, has agreed that these three papers satisfy its criteria concerning the required number of papers, the quality of journals in which the papers are published, and the issues of co-authorship.

This report will evaluate each paper in turn, in order of publication date, before giving a collective summary.

Stencel A. 2016: The Relativity of Darwinian Populations and the Ecology of Endosymbiosis. Biology & Philosophy 31 (5): 619–637.

Biology and Philosophy is a very well-respected journal which uses double-anonymous peer reviews and is the leading journal for the field of philosophy of biology. The paper is single-authored.

This paper proposes two very original and innovative ideas:

1) That we should treat a 'Darwinian population' as derivative from and relative to a Darwinian Individual;

2) That we should treat Darwinian populations as including organisms from different species.

The first thesis takes an idea developed by Peter Godfrey-Smith in 2009 and effectively turns it on its head. Godfrey-Smith articulates a Darwinian Population as a collection of living objects that meets Lewontin's evolutionary criteria of variation, heritability and fitness differences. The membership of the population is determined by fitness-affecting interactions between members, and membership is assumed to be transitive. If x is in the same population as y, and y is in the same population as z, then x is the same population as z.

For Godfrey-Smith a reproducer's capacity to participate in a process of evolution by natural selection is derivative from its membership in the right sort of population. It is a populational view, following in the footsteps of Ernst Mayr who argued that populations are the appropriate unit of analysis for evolutionary purposes.

In Mr Stencel's picture, instead, populations are not merely derivative, but have a much more fluid identity than in Godfrey-Smith's scheme. This is because the population is defined in terms of evolutionary interactions with a focal reproducer, so that different reproducers are members of different populations. What's more, the population associated with any one reproducer will be dynamic, its membership changing dramatically over time as different entities (other reproducers) come into interaction with it.

The second idea is that we include all the living things that are interacting, in a fitness-affecting manner, with the focal reproducer, as parts of its population, *regardless of their species.* This is in contrast to the standard way of defining a population which is as composed entirely of conspecifics.

One of the consequences Mr Stencel articulates is for our understanding of fitness. Because fitness is a measure of success in a particular environment, it can only compare conspecifics, or organisms which are 'exchangeable', a notion taken from Matthewson 2015. Two species are exchangeable if they are in competition for the same slots. Mr Stencel proposes that we still think of multispecies populations as undergoing natural selection, we simply refrain from comparing their fitness.

The main reason provided for moving to the revised view of a Darwinian population is that "it is hard to set the boundaries of a Darwinian Population". In particular, real-life cases often exhibit 'neighbour-structured' populations. This too is a notion developed by Godfrey-Smith, and is a contrast to 'group-structured' populations. Under group-structure, all members of a group interact, or at least have the potential to interact, with all other members of the group. Under neighbour-structure, instead, units interact only with their immediate neighbours in chains. Here the relationship is not transitive, so although x interacts with y, and y interacts with z, x does not interact with z. Mr Stencel argues that in such cases x, y and z should not be conceived as members of a single Darwinian population. Instead, we should treat each of x-z as having its own unique population comprised only of those reproducers with which it interacts directly.

Mr Stencel argues that his conceptual moves open up the possibility for better accommodating scientific work done on 'Holobionts' because reproducers from distinct species often interact in ways that affect one another's fitness, offering either boosts or costs to each other's ability to produce offspring.

I found this article tremendously stimulating and original. It clearly opens up novel ways of conceiving evolving entities, whose consequences are far from trivial. The paper is clear and generally well-argued. It is well supported empirically, and deals sensibly with anticipated objections. However, with theses as radical as these, it is inevitable to attract significant resistance and to leave many open questions. I explain my own resistance in what follows.

I note that the two parts of Mr Stencel's thesis are separable, and separately interesting, so we have two theses for the price of one, here. Each of them is fresh and exciting. The suggestion of treating populations as determined by the interactions relations of particular reproducers, as changing over time and as different for different reproducers, could be defended independently of the suggestion of including different species within populations. But the converse may not be true – it is hard to conceive how one could keep the traditional, population-first view, while expanding it to incorporate multiple species, without simply moving to something like an ecosystem view.

Regarding the first thesis – I wonder whether one might reply that what's needed it not a wholesale revision of our concept of the Darwinian Population, but only a realisation that in genuine cases of neighbour-structuring, there simply is no population above the scale of neighbourhoods. This would presumably be Godfrey-Smith's own position. Alternatively, one might seek solutions to the problem of defining populations objectively (as eg in Roberta Millstein's work). Page 624 reads "*Populations are not permanent structures created once and for all by an artisan-like demiurge responsible for the design and maintenance of the physical universe*" I don't think Godfrey-Smith suggests anything close to this. And everyone conceives populations such that they are dynamic – members die and are born all the time, of course, as well as migrating in and out.

Furthermore, one might accept the first thesis – that populations need to be defined relative to particular reproducers, and still reject the move to multispecies populations, I think. There is not a huge amount of argument for the second thesis. You say there is 'nothing wrong with' including multiple species, but ideally there would be more than this. I should like to know what is inadequate about existing frameworks, which treat other species as part of the focal species' environment. It is not as if standard evolutionary theory has no resources for accommodating symbiosis.

Furthermore, you say there is 'nothing wrong with' switching to a multispecies view, buy you identify some problems – eg the inapplicability of fitness measures. You say we can decouple selection from fitness, but how? how can we measure a selection differential, say, if fitness is out of bounds? What happens to the idea of evolutionary response?

Mr Stencel suggests that there is a problem with understanding the evolution of endosymbiotic transitions, because once engulfed a mitochondrion can no longer compete against or interact with free-living mitochondria. It is not obvious to me why this should be so. Mr Stencel declares the mitochondrion a part of the engulfing cell, rather than something which interacts in its own right, without explanation of what motivates that switch in perspective. Reasons need to be given for thinking of it as anything mind-independent. The mitochondrion still needs all the same metabolic resources as before, for example, and still competes with other mitochondrion for them. We might simply think of it as gaining the host's 'help' in accessing them. Apart from anything else, evolutionary transitions are unlikely to be as sudden as is implied. In reality it took many thousands of years, and the gradual evolution of many different traits, for mitochondria to become endosymbionts. Mere engulfment – the interposition of a cell membrane between a mitochondria and its environment – does not change so much.

I wondered at time whether Mr Stencel might be applying an overly narrow conception of a fitness-affecting interaction, as something that is very causally immediate, even requiring physical contact, perhaps. This yields different consequences from a view in which organisms can compete, for bananas say, without needing to ever occupy the same location as one another. Engulfment, on the latter perspective, is compatible with competing with free-living entities for metabolic resources. The narrower perspective would need to be defended.

One important question that is left under-examined in this paper concerns the identity and identification of reproducers. Eg on page 629 Mr Stencel says that all the cells in a cat make up one reproducer – but which cells? Are they ruled in by possession of a particular genotype, as assumed in the folk view? Or by mitotic development from a zygote? Upon what principle are we excluding, for eg, gut microbes?

Mr Stencel argues that we might need to refrain from attributing fitness to members of populations, on his view. It might be, however, that alternative conceptions of fitness could be made to work. For example, Van Valen conceived of fitness as rate of increase, in the long term, of biomass, without worrying about species identities. Cooper conceived it in terms of expected time to extinction. More attention to work in bacteriology may help too, because there the notion of species is vague and quantitiative anyway.

I also suggest looking into Toby Kiers' application of economic market theory to symbiosis. Species identity is not important here, only the product being 'sold'.

One issue that deserves reflection is this: The populational view is motivated by the need to abstract away from the particularities of individuals. Realised fitness is only expected to correspond to actual fitness on average. Mr Stencel's account does away with this, putting all the idiosyncrasies of concrete particulars back into the centre. At what cost? What difference will it make, for example, to our ability to make predictions? One might think that if all populations are local to a focal reproducer, that we may only use evolutionary theory to make predictions in a very limited, local sense? In fact, would we be able to make generalisations at all? We can't talk about the future of the population as a whole, because we are only concerned with a fragment of it. And we can't talk about the evolutionary future of a reproducer, because there is no such thing.

It is a very innovative and suggestive paper, opening up some new conceptual possibilities. It uses some very vivid and helpful examples, such as the chimps fighting with cats over bananas. It concludes that such research undermines one core concept - that of a Darwinian Population – but leaves other -the unit of selection, the organism -intact. But the paper is largely suggestive. For example, it is entirely informal. The new 'reproducer's eye view' would require complete revisions of the standard maths used to understand ENS. Does Mr Stencel plan to provide that later? Only when that is done can we truly evaluate claims such as that the new system will be 'more precise'. Philosophers are supposed to be suggestive of course, and one of the most cognitively demanding tasks is to see beyond current theory to imagine alternative possibilities. However, I would have liked to have seen more done, here, to work out the likely consequences of the radical conceptual shift being proposed.

<u>Stencel A. and Proszewska A. 2018: How Research on Microbiomes Is Changing Biology: A Discussion on the Concept of the Organism. Foundations of Science, 23: 603–620.</u>

This paper explores the question 'Does holobiont research require us to change our idea of organismality?' The answer given is that it depends upon which definition of organismality we are using. Two definitions are evaluated. The developmental concept does conflict with holobiont research, but Queller & Strassmann's cooperation/conflict concept does not.

This paper is less constructive and original than the first, but it asks sensible questions and contributes to the field by working through the answers. I think that the results are somewhat idiosyncratic – different authors posing the same questions might arrive at different conclusions about the fit of holobiont research with the two approaches explored. This doesn't undermine the more general conclusion, however, which is that because different definitions of the organism are permissible, there cannot be any simple account of the challenge posed by Holobiont research.

The interpretation of a developmental definition of the organism is idiosyncratic in that, rather than looking to what proponents of developmental biology themselves write about organismality (people such as Paul Griffiths in Developmental Systems Theory; Jim Griesemer's account of reproducers or even Scott Gilbert's), the authors interrogate their own intuitions, and decide that a developmental view must be one that defines organisms as developing by mitosis from a zygote.

What the paper shows is that if you pick out the unit that develops by mitosis from a human zygote, then the result is not a unit of function. This is true, and interesting, and worth explicating. But this is not what the authors take themselves to show. They argue that a developmental definition is left untenable. I cannot see any reason why a developmental definition cannot remain. One reason is that a developmentalist could define the unit of development as including anything needed to acquire the normal healthy phenotype. Alternatively, even assuming we understand the developmentalist view as defining an organism as all the mitotic products of a zygote (this was TH Huxley's idea, originally), all this commits us to is the conclusion that developmentalists do not treat the organism as including symbiotic microbes. One would need to draw on further argument to explain if and why this cannot be done. Once you invoke functional ability, you are not confining yourself to a developmental definition any more.

To put it another way, definitions can never be falsified by pointing to things that they don't include. Definitions are supposed to exclude things, after all. You can at most argue that a definition should not be used, by giving reasons why the exclusions are inappropriate. What you might try to argue, therefore, is that Huxley's definition shouldn't be used because the units it picks out exclude things that are functionally essential…….and things that are functionally essential must not be excluded! But you need to give a reason. I suspect Huxley wasn't trying to capture the unit of function. Huxley's view comes apart from a functional view in several cases already well known eg eusocial insect colonies, identical twins (Julian Huxley rejected TH Huxley's view for that reason).

I also had some worries when it came to Queller and Strassmann's account. It wasn't clear that the authors understood that Queller and Strassmann's account is fundamentally an evolutionary account. When they talk about cooperation, for example, they intend the technical biological definition of cooperation = a trait that has evolved because of its effects on the partner. This comes apart from more colloquial, proximate ways of understanding cooperation. For example, to establish cooperation in the biological sense the partners should exhibit some evidence of co-evolution, such as genome reduction. This is there for some symbiotes, but not for many others! Queller and Strassmann say as much in their 2016 paper.

It would have been helpful to appeal to work on different ways of contributing to development, as found in literature on Developmental Systems Theory and the parity thesis ((Griffiths, Woodward 2010; Stegmann 2014). Woodward's distinction between Instructive versus permissive causes might be especially helpful (Woodward 2010). Some causes are more specific – specific changes in input produce specific changes in output. Others make a difference between output and no output at all, or only vary quantity, not quality of output.

p. 614 Discusses pluralism. I picked up some potential inconsistency here. The idea of there being both broad and narrow approaches – isn't it assumed that they are approaches to the same thing? I would like a clearer statement saying whether the authors think there is an underlying reality that explains why different aims are served by different conceptions, or whether they think that anything goes.

I would also have appreciated hearing more support for the modish ambition of attending to scientific practice rather than (presumably) theory.

The authors did not here convince me that any definition must be abandoned, in light of holobiont research, but they did succeed in exposing some important pressure points: issues in regard to which researchers confront a difficult choice.

<u>Stencel A. and Włoch-Salamon D. 2018: Some Theoretical Insight into Hologenome Theory of Evolution and the Role of Microbes in Speciation. Theory in Biosciences, 137: 197–206</u>

This paper argues that most holobionts are not units of selection, but that they can be usefully treated as units that are evolutionarily significant, using Queller & Strassmann's schema of cooperation and conflict. The authors then use this to accommodate a theory of speciation by divergence of symbiotes.

It draws a bold and fascinating conclusion: that we are obligated to take units of cooperation seriously, even when they do not coincide with units of selection, because we depend upon them for explanation of a particular mode of speciation.

In general it is a pleasure to read, being well written and very thought-provoking. The point about holobionts not being units of selection – though not original to these authors – is well explained. The central argumentative strategy, invoking IBE, is very solid and I am very much sympathetic to it. *Here is a valuable theoretical role. This concept of the individual is needed to support that role. Conclusion – we should take that concept of the individual seriously.* I did wonder, however, how well this fits with the content of the former paper, which prioritised practice over theory and took a more pluralistic stance.

Here are some aspects of the paper that left me feeling (pleasantly?) disorientated.

I have the same worry here that that Queller & Strassmann's account is being interpreted in an overly proximate sense. Queller & Strassmann's 2016 paper 'Problems of multispecies organisms' explicitly says that complex holobionts do not fit their concept of the organism, in terms of cooperation and conflict. In general, Queller and Strassmann's concept is not an alternative to a unit of selection or 'Darwinian Individual', rather, it is their way of making the evolutionary concept more precise.

So it is difficult to see what the authors have in mind. My best guess is that they are interpreting cooperation purely functionally/proximately. Ie a trait is cooperative if it benefits the partner. The resulting concept of the individual would be much closer to Dupre and O'Malley's metabolic individual, or indeed to a simple functional definition, than to Queller and Strassmann's.

But there is a problem. Several accounts pick out the unit the authors are aiming at (metabolic, functional, immunological, for eg). But I think the authors need the more demanding notion of cooperation to underwrite speciation. For hybrid sterility to occur, incompatible symbionts will do. But for two lineages to speciate on the basis of this, is much more demanding – the two lineages need to undergo differential adaptation. If the symbiont-host relation is contingent and variable, because symbionts are transmitted horizontally, then it is hard to see how speciation will come about. Speciation on the basis of symbionts requires the symbionts to be parts of the unit of selection/Darwinian individual.

Here is one reason: If we say that speciation occurs as a consequence of possession of different horizontally transmitted symbionts, it seems we would have to accept de-speciation also – as when the hybrid mouse had its health restored by antibiotic treatment. Speciation is not standardly conceived of as being reversible, because it should depend upon irreversible genetic changes in the organisms. The host organism can only evolve genetic changes in response to its symbionts if those symbionts are acquired with high heredity.

The tube worm example is well chosen, because it has signs of co-evolution with its bacteria even though they are horizontally transmitted. The authors emphasize the way the worm plays 'crucial roles' ie functional integration, but I would say that what is most relevant about the worm, for Queller & Strassmann's purposes, is the way it has co-evolved with its bacteria. For Queller and Strassmann this provides evidence that the relationship is very robust, even if the bacteria are not inherited vertically. I would guess that because the bacteria are concentrated in the thermal vent, where there food supply, it is easy for the worm to be confident of finding new partners, just by staying near to the vent. We might wonder if the same is true about squid-vibrio. Even though the bacteria are taken up anew each time, the squid have clearly been sufficiently 'confident' about being able to access new bacteria reliably that they have evolved special compartments. What is interesting about this, to me, is that it tells us vertical transmission is merely one mechanism by which symbiotic partners can interact with sufficient durability that a response to selection can occur. Other mechanisms, such as niche construction and maternal effects, are given insufficient attention. What matters, in terms of the expectation of an evolutionary response, is heredity, regardless of how it is secured.

I would love to see more exploration of which holobiont members are passed on with sufficient heredity for mutualistic co-evolution to have occurred, and also of what mechanisms those partners use to create that heredity (or what ecological factors underwrite the heredity). You say "the majority of microbes within a given host are not sufficiently integrated into that host to enable it to be considered a collective reproducer." I suspect you'd find that most of the microbes also fail to meet the condition of being acquired with sufficient heredity for an evolutionary response to occur. If that's true, then we don't need the holobiont concept to explain symbiote-mediated speciation, we still only need a more restricted Darwinian Individual concept, and we still don't expect symbiotes to support speciation outside of a narrow range of cases in which symbiotes are re-acquired with high heredity.

On the other hand, an explanation of the speciation seems available that is at odds with both the authors' own unit of functional cooperation view, and with a some-symbiotes-as-parts-of-the Darwinian-individual-view: Suppose that we treat the mice and parasitoid wasps in a traditional fashion, as including only genetically homogeneous cells, or products of a zygote. Then we treat the symbiotes as just one of many essential resources in its environment. Compare: two subpopulations of birds come to rely on different food sources, and their beaks diverge to cope with those food sources. Hybrids may then end up with beaks that cant manage either food source. Can we not say the same about the wasps and mice? They are adapting to different microenvironments. The only special factor is that the relevant part of the environment is internal – but that shouldn't be so radical. The issue for the mice seems to be not so much that the mice have adapted (or the problem wouldn't be reversible with antibiotics) as that when the symbionts are mixed they fight and fail to produce the benefits upon which the host has come to depend. If we don't require a new conception of organism which includes food sources as parts of the organism, in order to explain the bird speciation, then why do we need a revised concept that includes the symbionts?

Perhaps the point is this – speciation often happens in response to things that are external to the organisms themselves – new rivers, for example. Why not think of the symbionts as just another such factor?

Finally, I have general worries about the sort of concept which relies on causal interaction and/or functional autonomy to pick a unit out – in particular, what stops it from being absurdly over-inclusive. This worry attaches to the Stencel 2016 paper also. The tubeworms have no digestive tract, because they rely on bacteria to digest sulphur for them. Humans have no photosynthetic ability because we rely on plants to produce oxygen for us. dependence is everywhere. No organism is independent. Ecological webs are universal. Where is the stopping point? Is there some sort of threshold or quality of interaction to delimit things at non-universal scales (But what? is it measurable?) Or is there only one true living unit – the whole planet/Gaia/the universe? Eg Subrena Smith seems happy to accept the latter as just the way things are. But I think it rather undermines the usefulness of the notion of a unit.

In sum, this paper does what all the best philosophy papers ought to do – leaves the reader wrestling with fundamentals and struggling to put the world the right way up again. The paper is fantastically thought-provoking and opens up an important class of questions, and draws attention to the fact that vertical inheritance is over-emphasized as a mechanism for evolutionary individuality.

General summary

The articles are very well empirically informed, distilling a huge wealth of biological insight and detail in a way that is interesting and accessible to the reader, without being overwhelming. The examples are well chosen and are not simply the same case studies that every other author writing on holobionts uses – effort is made to do the research necessary to find and understand the biology in the right amount of detail for an effective case to be made. A properly through appreciation of holobiont research is on display, as well as of evolutionary theory more generally, and the traps of over-simplification and over-generalisation are avoided. At the same time, the articles are impressive in their philosophical sophistication, show plenty of knowledge regarding theories of individuality, and never stray into the territory of merely reporting scientific developments without offering any additional analysis. Neither do they indulge in hyperbole or exaggeration – it would be a wonderful thing if every article written about holobionts were offered the same level of careful and rigorous scrutiny on display here.

Stencel and Wloch-Saloman applies sophisticated philosophical methodology, ie if you want to determine the nature of a scientific kind, you should explore the roles the kind is required to play in scientific theory. Stencel 2016 is the most innovative and independent, offering a radical and fresh new perspective on Darwinian populations, but all three papers are rich in theoretical knowledge and philosophical insight. One questions concerns the relations between the different papers. The 2016 article presupposes that we can identify reproducers. The others show how holobiont research causes problems for the task of defining a reproducer, but without ever arriving at a determinate answer. I should like to know whether Mr Stencel broadly thinks that we could have reason for favouring any view, over others. If not, doesn't this leave the task of delineating a Darwinian Population in rather worse straits than suggested?

The over-arching question of the thesis is whether research on symbiotic microorganisms necessitates a changed understanding of population biology. I wouldn't go so far as to say that the articles have convinced me of a positive answer to the question, but they did succeed in providing sophisticated challenges to what we might call the folk view of the organism, as something which is genetically homogeneous, develops mitotically from a zygote, and autonomously performs all the functions necessary to its own survival and reproduction. They succeeded, furthermore, in leaving me with a wealth of interesting questions and important realisations that need further exploration. I very much look forward to reading much more of Mr Stencel's published work in the future.

I have no hesitation in recommending Mr Stencel for the award of a Doctorate, based on this work.

1) Theoretical knowledge
2) Ability to independently carry out research
3) Originality of solutions

The submitted dissertation, in the form of three articles published in peer-reviewed journals, shows the candidate's theoretical knowledge in the field of Philosophy and testifies to the candidate's ability to independently carry out research in Philosophy.

The dissertation offers an original solution to a Philosophical problem.

Accordingly, the submitted word fulfils the requirement for a doctoral dissertation, as stated in the Polish Law on Degrees in Science, Art and Humanities from March 14th 2003, art 13 ust.1.

Sincerely,

Ellen Clarke