

Dear Dr. Vacher,

Thank you very much for your detailed review of our manuscript. Please find below a list of responses to your comments/changes in addition to a version of the text with tracked changes. We hope that this revised version of the manuscript now meets your expectations. Kind regards and thanks again for your efforts,  
Simon Dittami.

C1: These two aspects could be presented as specificities of marine ecosystems

→ done

C2: This is too vague. Future research axes need to be specified

→ " e.g. the development of controlled experimental model systems for holobionts from all major lineages and the modeling of (info)chemical-mediated interactions between organisms " was added

C3: This can be removed to save space

→ done

C4: Please give a few examples of relevant model systems and relevant approaches

→ See addition in response to C2.

C5: Please give some examples of concrete applications

→ "e.g. to increase yield or disease resistance in aquacultures or to protect and restore marine ecosystems through management projects"

C6: Please include one or two key references for every definition of the glossary.

→ done

C7: The reference of the book should be included.

→ done

C8: Please briefly explain how gnotobiotic systems are obtained. Explain the difference with "germ-free" systems.

→ done

C9: Why is evolutionary into brackets? Please include one sentence and one reference to mention the debate on this topic.

→ "Whether or to what extent holobionts are also a unit of evolution is still a matter of debate (Douglas and Werren, 2016)" was added.

C10: To be replaced with holobiont?

→ done

C11: "Russian dolls" could be used to explain the concept of nestedness. This would make a link to Figure 2.

→ done

C12: Add one sentence to give examples of phagocytosed cells.

→ "e.g. the uptake of bacteria by sponges (Leys *et al.* 2018)" was added

C13: Parasitic relationships are not included in the definition of symbiont (above). The two definitions should be consistent

→ The definition of symbiont referred to symbiosis, so parasitic relationships were also included. This is now explicitly mentioned.

C14: This section should be structured in chronological order. Dates and influential scientists in the field need to be made clearer.

→ The philosophical concept of holism was now moved to the beginning, and important contributions and dates were underlined.

C15: The terms "symbiont" and "symbiosis" are defined in the glossary. "Symbiotic" should be in bold, or you could change the sentence to use first "symbiont" or "symbiosis"

→ We had previously used bold formatting to highlight themes as help the reader to navigate the paper (in response to the first round of review). We now use boldface for terms in the glossary instead, as requested.

C16: The term phagocytosis (in the glossary) should be included in this paragraph.

→ done

C17: Why is it in bold? This is not in the glossary.

→ see C15

C18: The name/date of the theory and the main protagonists should be mentioned in the previous paragraph.

→ Mereschkowski (1905) and Wallin (1925) were added.

C19: This term should be bold, it is defined in the glossary. Please check that the terms defined in the glossary appear in bold the first time they are used.

→ done (see C15)

C20: To be defined in the glossary

→ done

C21: What is the nature of the interactions within holobionts and across holobionts? Please give some examples of interaction types.

→ "such as induction of chemical defenses, nutrient acquisition, or biofilm formation" was added.

C22: Within holobionts or across holobionts?

→ We now specifically state "across holobionts".

C23: What do we know about microbial fluxes across marine holobionts? Have they been measured?

→ We are not aware of any publications measuring microbial fluxes across holobionts directly, this was now clearly stated below in the community assembly section.

C24: The whole paragraph should be re-structured to better highlight the main differences between marine and terrestrial holobionts. The differences are more clearly stated in the responses to comments: “The two main differences between marine and terrestrial holobionts we have identified are the high level of connectedness of habitats and the diversity of phylogenetic lineages”

→ We hope that the modifications now make the differences we found sufficiently clear.

C25: To be defined in the glossary.

→ done

C26: Where are the limits of the holobiont under this definition? This should be explained.

→ we now added “setting the boundaries of the holobiont depending on the interactions and biological functions that are being considered”

C27: This definition should be moved to the glossary.

→ done

C28: What is complex? The concept of holobiont or the holobiont? This sentence is too vague and should be rephrased.

→ we now state more precisely: “Thus, the holobiont concept and the underlying complexity of holobiont systems should be further considered when addressing evolutionary and ecological questions”

C29: A few pictures of the main marine holobiont models could be included.

→ This was partially the aim of Figure 1, which now cited here, also.

C30: Please explain what “environmental model” and “semi-controlled model” mean.

→ We now added “*i.e.* holobiont systems in which microbiome composition is not or only partially controlled”.

C31: This definition could be moved to the glossary. The difference with “gnotobiosis” should be explained.

→ done

C32: To be defined in the glossary. The section could then be structured according to the main processes. The link to the previous section on model holobionts should be clarified.

→ “Ecological processes” was added to the glossary. The section contains three subsections: “dispersal”, “sustaining biodiversity”, and “biochemical cycles”. A link to the previous section has been made: “Work on model systems has demonstrated that ...”

C33: The term “assembly processes” should be defined in the glossary. Vellend’s four processes for community assembly could be used to structure this section.

→ It is interesting to see this from an ecological perspective – most of the literature on holobionts merely looks at horizontal vs. vertical transmission, with selection vs. drift being the key factors. We now clearly identify all 4 processes in the text, although we have much more information on selection.

C34: In Figure 3, predictive modelling is associated to large-scale studies, while mechanistic understanding is associated to the study of model holobionts. This should be stated in the text.

→ done: "we identified two distinct opinion clusters: one focused on mechanistic understanding and work with model systems and another one around large-scale data set analyses and predictive modeling"

C35: A figure linking the emerging methodologies and the future research axes would be useful.

→ done, see Figure 4

C36: The term "biomonitoring" could be introduced here and defined in the glossary.

→ done

C37: The term "biocontrol" could be introduced here and defined in the glossary.

→ done

C38: The term "biostimulation" could be introduced here and defined in the glossary.

→ Biostimulation is frequently used in the sense of adding nutrients to foster the growth of microbes that can degrade toxins or contaminations – using this word in another sense here may lead to confusion.

C39: A list of priority research questions, indicating the biological models and emerging tools that are appropriate to address them, seems to me essential for the paper to become a reference in the field.

→ done: "Accordingly, current key questions in marine holobiont research cover a wide range of topics: What are the exchanges that occur between different partners of the holobiont, and what are the cues and signals driving these exchanges? What are the relevant units of selection in marine holobionts? How do holobiont systems and the interactions within them change over time and in different conditions? How do such changes impact ecological processes? How can this knowledge be applied to our benefit and where do we need to draw limits? Identifying and consolidating key model systems while adapting emerging "-omics", imaging, and culturing technologies to them will be critical to the development of "holobiont-aware" ecosystem models."

C40: What are the differences between the three pictures of archaea? I can't see them. I think that all these small pictures could be replaced by a few bigger pictures of model holobionts.

→ Another picture of archaea was added, but the image size represents a compromise between showing the actual organisms and illustrating the enormous marine diversity, which is why we would prefer not to reduce the number of images.

C41: The position of viruses in the middle of the circle give the impression that they lack host-specificity.

→ Viruses were moved to the outer circle

C42: The nature of the interactions should change when considering larger spatial and temporal scales.

→ These changes are now explicitly mentioned in the legend

C43: The term “dysbiosis” could be introduced in the figure.

→ The term is now explicitly mentioned in the legend (see C42)

C44: Horizontal (4) and vertical (5) transmission of microorganisms could be represented as network links.

→ Examples of this are now shown as arrows in the figure.

C45: Predictive modelling is associated to large-scale studies, while mechanistic understanding is associated to the study of model holobionts. You could circle each cluster and give a title to each approach, and better highlight the node “potential use, management” that corresponds to the common goal.

→ Adding even more lines to the figure significantly decreases readability. This is why we opted for a color code to highlight the two clusters. “Potential use, management” already stands out by its connectedness to both clusters. It is one but not "the" common goal, and we do not see a convincing reason to promote it to a higher level than the other keywords. We used the size of the nodes to give different emphasis to the keywords according to participant votes and would like to keep these values, hoping that they are representative of the community.