LETTER

REPLY TO DAYBOG AND KOLODNY:
Necessary requirements for holobiont-level selection are robust to model assumptions

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Daybog and Kolodny (1) extend our multilevel selection model for host–microbiome dynamics (2) by using a nonlinear relation between helper frequency and host fitness. They use a step function where host fitness increases 19-fold when the helper frequency reaches 1% and compare this to our linear response where host fitness increases 2-fold when the helper frequency reaches 100% (and increases 1.01-fold for a 1% helper frequency). Daybog and Kolodny thus make extreme assumptions about host fitness. They find that holobiont-level selection is possible in a larger part of parameter space and argue that our previous conclusions cannot be generalized. However, Daybog and Kolodny's findings do not invalidate our main conclusions.

In ref. 2, we show that holobiont-level selection has two requirements: 1) the ratio of the timescales of microbial evolutionary dynamics to host population dynamics should exceed a threshold value; and 2) the ratio of vertical-to-horizontal transmission should exceed a threshold value (2). The magnitude of these thresholds depends on the model assumptions, as shown by Daybog and Kolodny and our previous work (ref. 2, SI Appendix figure S1). However, for all systems the applicable thresholds need to be exceeded, because hosts vary in fitness only when condition 1 is met, and host fitness is heritable only when condition 2 is met (2). Daybog and Kolodny's work highlights the generality of these conclusions: Even under their extreme assumptions, holobiont-level selection can only act when both conditions are met (ref. 1, figure 2, upper-right corner*).

According to Daybog and Kolodny, we claim that "the parameter space [for holobiont] selection [. . .] is extremely restricted." This misrepresents our main conclusion (we use the term "stringent conditions"). We show that holobiont-level selection only occurs if the two conditions described above are met. We call these conditions stringent, because for many animals horizontal transmission is stronger than vertical transmission (3, 4), and because generation times of hosts and microbes can differ strongly (5). Estimates of holobiont-level selection in nature should be based on parameters and fitness functions found in natural systems (rather than on particular model assumptions).

Finally, Daybog and Kolodny state that we use an "unusual combination of hard and soft selection," but this mischaracterizes our multilevel selection model, for which the terms "soft" and "hard" selection may not be applicable. In our framework, individuals with the highest relative birth rate are favored at both the microbe and host levels; hence selection could be considered "soft" at both levels.

We agree with Daybog and Kolodny that it is important to further explore how alternative mechanisms, such as nonlinear fitness functions and host feedbacks (as we point out in ref. 2), affect holobiont level selection, and their work highlights the utility of our framework in addressing these questions. However, these effects are unlikely to alter the necessary conditions for holobiont-level selection: The relative strength of vertical and horizontal transmission and the relative timescales of microbe and host dynamics are likely important measures in any system.

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*In the lower-right corner, helpers are maintained by stochastic fluctuations and not selection (see ref. 2).

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