Response to reviewers: Mutualists construct the ecological conditions that trigger the transition from parasitism

Ledru et al.

We would like to thank the reviewers for a thorough and thoughtful review to the manuscript titled 'Mutualists construct the ecological conditions that trigger the transition from parasitism'. We have worked on addressing the reviewers' comments and believe that the paper has significantly improved as a result. Since some comments are redundant, we refer to other comment's responses in our answers. Below, you will find the reviewers' comments in black, and our responses in blue. The line numbers in our responses refer to the revised manuscript.

1 Reviewer 1

1.1 General comments

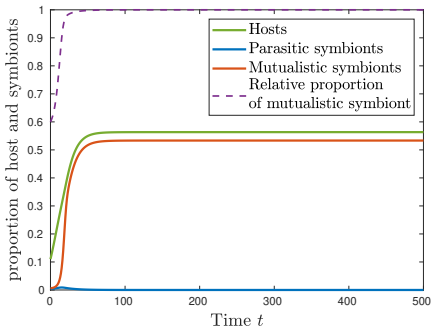
An interesting preprint with great ideas and results. Dear authors, four referees have reviewed your ms. Based on their remarks and my own reading, I would like you to revise your paper before I can recommend it. Overall, I was very pleased to read your manuscript as it is very rich in terms of both biology and theoretical results. The way you present the goals of the study as well as the background / state-of-the-art is helpful to understand where you are going. Thank you for the excitement!

1.2 Analytical approximation

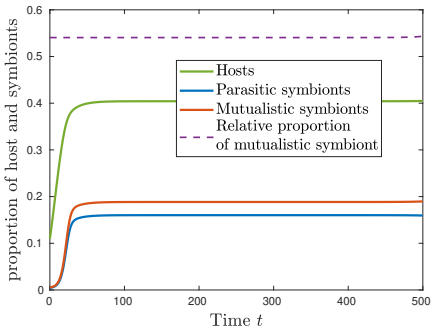
One of my main concerns comes from the fact that you plunge right into the simulation model without trying to give some rough predictions based on some analytical approximation of the model. Considering global dispersal, some computations can be done, e.g. finding the proportion of cells occupied by hosts at "equilibrium" (I found 1-sqrt((1/f)*(m/(1-m))) because the way you formulate P_I and the fact that a cell must be unoccupied to be colonized make the density-dependence squared). Such an equation is interesting because it yields the occupancy of the grid when parasites are absent (64%) or present (20%), which set the limits for what you expect when evolution comes into play. You can also compute population growth rate using Euler-Lotka equation – this would help you justify why the host population is viable in the absence of mutualistic symbionts, etc. I do appreciate the importance of a simulation model in the present case, but it is very difficult to be surprised or not surprised at the results if one has absolutely no clue as to what would be predicted by a simpler, approximated analytical model.

Thank you for this methodological remark which helps us to improve the heuristics formulated in our manuscript. Based on our stochastic model, we build three models based on deterministic recurrent equations. Our main idea is to consider the evolution of the proportion of occupied site by hosts and symbionts when they disperse globally over a landscape composed of N sites. We detailed our model and the mathematical analysis in the appendix A2 "Mathematical approximations". In this appendix, we derive quantitative and qualitative description of the models, which give insights on the the stochastic model. In particular, we first justify our parameter range by showing that they allow parasitic system persistence Moreover, we predict the amount of host and symbiont in this parasitic system. Secondly, we discuss the competitive exclusion process between mutualistic and parasitic symbiont in absence of mutations. Finally, we show that mutations only maintain a very small proportion of mutualistic symbiont in the parasitic system around 2%. Finally, those simple models help us to motivate the 10% threshold above which we assume mutualism has emerged (see our response to comment 2.9 and 3.17).

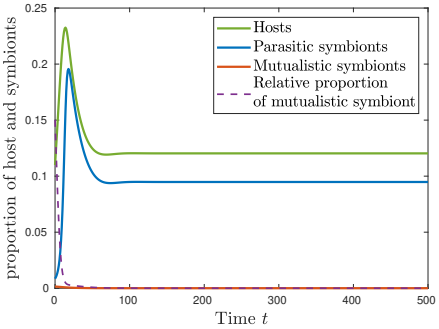
In our manuscript, we include the following additional information:
Appendix A.2 "Mathematical approximations". We present the following three models.
- Approximation of the parasitic system
- Approximation of the mutualistic/parasitic system without mutations.



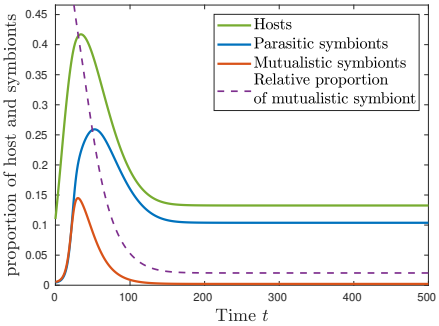
(a) Without mutation and $p = 0.6$



(b) Without mutation and $p = p^*$



(c) Without mutation and $p = 0.15$



(d) With mutations and $p = p^*$

Figure 1: A8 – Evolution over time of the host-symbiont model (20) (panel a-c) and (22) (panel d) with two types of symbionts: parasitic symbionts ($\alpha_s = 0$) and mutualistic symbionts ($\alpha_s = 1$). We present the model (20) without mutation for various initial relative proportion of mutualistic symbiont p: (a) $p = 0.6$, (b) $p = p^* \approx 0.45$ and (c) $p = 0.15$. The model (22) with mutation is presented in (d) with initial proportion of mutualistic symbiont $p = p^*$.

– An approximation of the mutualistic/parasitic system with mutations.

Moreover, we include the following sentences in the main text:

line 195 page 5 in "Parasitic system and transition" :

"To tackle the issue of transition to mutualism, we assume that the system is viable without mutualism (see appendix A.2 for details). More precisely, in the absence of mutation, the extinction probability of a population with parasitic global dispersers without dispersal cost (minimal interaction traits, $\alpha_s = \alpha_h = 0$, dispersal trait $\varepsilon = 1$ and dispersal cost $d = 0$) is given by $m/\big((1-m)f^a\big)$ where m is the mortality rate and f^a the fecundity of a parasitic host without symbiont. We choose parameters such that the extinction probability is less than 1. In this case, the population stabilizes around a demographic equilibrium called the "parasitic system" where host density is around 0.15 and the symbiont density is around 0.1 with parameters value set in Table 1 (see Figure 2b-c and appendix A.2). From our perspective, this situation is the worst-case scenario because interactions are parasitic and dispersal cost is minimal. Then, mutualistic symbionts can appear by mutation, which generates approximately 2% of mutualistic symbionts in the population (see dashed purple curve in Figure 2c and Figure A8d). Natural selection eventually leads to a significant increase of the percentage of mutualistic symbionts, far above the 2% generated by mutations (Figure 2). Using an approximation model, we show that the extinction probability of mutualistic symbionts falls below 1 when the percentage of symbiont rises above 10% (appendix A.2 for details). In the simulations, a high density of mutualistic symbionts indeed persists in the long term when the percentage of mutualistic symbionts stands above 10% (Figure A9), which therefore characterizes the transition to mutualism. The transition time was defined as the time at which the percentage of mutualistic symbionts rises above this threshold."

1.3 Mutation model

As remarked by at least one or two referees, the mutation model looks strange. As all the traits you want to have evolve are between 0 and 1, why don't you use beta distribution (or logit Gaussian) for mutation? The issue with truncated exponential is that the closer you get to the trait boundaries, the less likely mutation swill be accepted. So you would get an acceleration of mutations at mid values, and this could be problematic. The beta distribution looks like the cleanest contender for a mutation distribution in [0,1] and you can always specify it so that it looks hump-shaped rather than u-shaped.

Response:

We agree that our mutation model was unusual and we fix this. The main issue with the exponential distribution is the risk to produce an offspring with a trait outside its range $[0, 1]$. In our previous model when such mutation occurred, it was cancelled. To minimize this issue, we replace our mutation kernel with a Beta distribution kernel with shape parameters $(1, 3)$.

Indeed, using a beta distribution with shape parameters $(1, 3)$ to describe the effects of mutations seems interesting because the support of the beta distribution remains in $[0, 1]$, thus it only produces mutations with finite size. In our simulation we constraint the maximal effect of mutation to remain below β_{max}

However, the beta distribution does not solve the issue of offspring with trait outside the range $[0, 1]$. Indeed, parents with trait close to the range boundaries are more likely to produce offspring with trait outside the range. In our previous simulations we just reflect the mutation so that it remains in the trait range. But this assumption biases mutations in favour to moderate traits. To fix this issue, we make the mutation kernel depend on the trait of the parent. In particular, if we sample an offspring trait outside the trait range then the mutation is canceled and the offspring inherits the trait of its parent. From a model perspective, the distribution of the effect of mutation is composed of truncated Beta distribution centered at the parent trait plus a Dirac distribution at the trait of the parent.

Many other alternatives would have been possible. For instance, killing offspring with trait outside the range would model deleterious mutations with large effect. This assumption is somehow similar to increase mortality due to the death of offspring with a deleterious mutation.

Another alternative would be to consider mutation effect distribution independent of the parents' trait, using for instance a uniform distribution to defined the trait of offspring. This assumption fixes our issue. It is similar to the house of cards assumption made in quantitative genetics to model a situation where mutations have really strong effects. In addition, it represents an "easy" situation for the emergence of mutualism. Indeed, if the trait of offspring is sampled uniformly in the range $[0, 1]$, then strongly parasitic parents $\alpha_s \ll 1$ may rapidly generate a strongly mutualistic offspring $\alpha_s \sim 1$. Under this assumption, our model becomes close to many models of the evolution of cooperation (altruism or mutualism) where only two extreme traits are considered: cooperative versus non-cooperative. However, in the present work, we aim to deal with a continuous interaction trait which draw an interaction diversity from a strongly parasitic agent to a strongly mutualistic agent. Moreover, we aim to deal with evolution where the distribution effect of mutation depends on the trait of the parents, and mutations with small effects on average. Thus we need several mutations - and therefore several generations - to go from a strongly parasitic individual to a strongly mutualistic individual. In addition, we expect this assumption to facilitate the transition from parasitism to mutualism. Indeed, we investigate the effect of the maximal size of mutation β_{max} on the transition (see Fig. A4). We can see that a larger maximal mutation size favours the emergence of mutualism (Figure A4).

In the manuscript, we reformulate the paragraph "Mutation in the Methods to clarify this point:

line 173 page 4

"Offspring inherit traits from their parents with variability due to mutations. The effects of mutations on each trait are independent . However, the distribution of mutation effects does depend on the trait of the parents. We use a Beta distribution with shape parameters $(1, 3)$ to describe the amplitude of these effects, which could be either beneficial or detrimental. This mutation kernel allows for rare mutations with large effects. However, these effects can not exceed a maximal mutation size set to $\beta_{max} = 0.5$ (see Figure A3 in appendix A.1 for details)."

We also add a paragraph "Distribution of mutation effects" in the appendix A.2

line 647 page 18

"During reproduction, individuals generate offspring with traits that can deviate from their traits due to mutation. The effects of mutation on each trait are independent. However, the mutation effect does depends on the trait of the parent. For instance, an individual with trait α will give birth to an

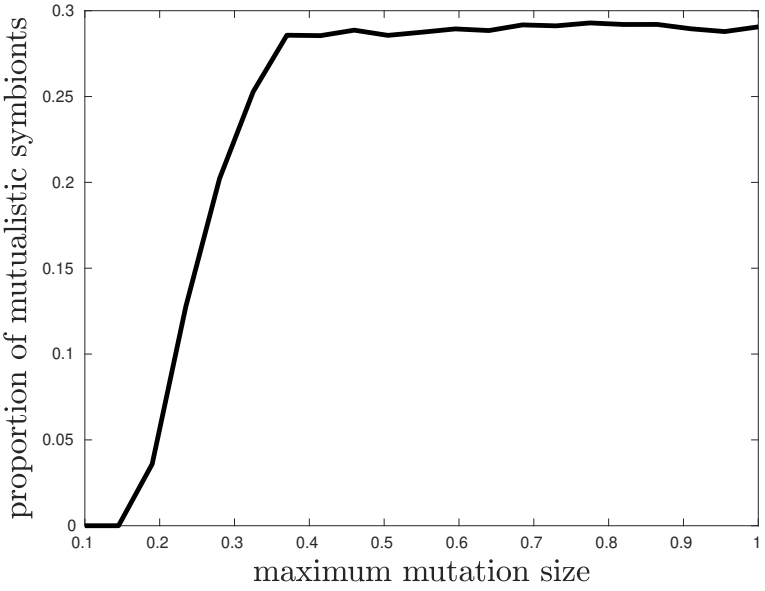


Figure 2: A4 – Effect of the maximum mutation size B_{max} on the proportion of mutualistic symbionts.

individual of trait $\alpha+\beta$ where β is drawn from a distribution with probability distribution function given by $K(\beta\,|\alpha)$, which depends on the trait of the parent α (Figure A3). In our model, we use a modified Beta distribution with shape parameters $(1,3)$ to describe the effects of the mutation. More precisely, for a parent of trait α, the effect of mutaion is a random variable β defined by

$$\beta = (\beta_{max}\,\xi\,B)\mathbf{1}_{0\leq\alpha+\beta_{max}\,\xi\,B\leq 1}$$

where B is a random variable, which follows a Beta distribution, ξ is a random variable independednt of B, which follows a Bernouilli distribution ($\mathbf{P}(\xi=1)=\mathbf{P}(\xi=-1)=1/2$). In other word, the random variable β follows the probability distribution function $K(\beta\,|\alpha)$, with $\alpha\in[0,1]$:

$$K(\beta\,|\alpha) = \frac{3}{2\beta_{max}^3}\big(\beta_{max}-|\beta|\big)^2\mathbf{1}_{|\beta|\leq\beta_{max}}\mathbf{1}_{0\leq\alpha+\beta\leq 1} + K_0(\alpha)\delta_{\beta=0} \tag{1}$$

where $\mathbf{1}$ is the indicators function, δ is the Dirac mass and the function $K_0(\alpha)$ is defined by

$$K_0(\alpha) = \begin{cases} \dfrac{1}{2\beta_{max}^3}(\beta_{max}-\alpha)^3 & \text{if } \alpha\leq\beta_{max} \\ 0 & \text{if } \beta_{max}\leq\alpha\leq 1-\beta_{max} \\ \dfrac{1}{2\beta_{max}^3}(\beta_{max}-1-\alpha)^3 & \text{if } \alpha\geq 1-\beta_{max} \end{cases} \tag{2}$$

Moreover, we investigate the effect of the maximal effects of mutation β_{max} on the proportion of mutualistic symbionts. From our formula, we know that the mean effect of mutation depends on the trait of the parent α but it is proportional to β_{max}, and it ranges between $3\beta_{max}/8$ for parents with intermediate trait ($\alpha\sim 0.5$) and $3\beta_{max}/4$ for parents with trait either close to 1 or 0. We show in Figure A4 that increasing the mean effect of mutation increases the proportion of mutualistic symbionts in the population. Thus large effects of mutation favour the emergence of mutualism. In our simulations we fix the maximal effect of mutation to $\beta_{max}=0.5$."

1.4 Reproduction with Poisson distribution

The reproduction process also looked strange to me since you basically use the integer part of f as a given (i.e. you fix the number of offspring) and then us e the decimal part as a stochastic bonus. Why didn't you use a more classic approach such as drawing from Poisson distributions? Effectively, the variance in offspring number is very low in your simulations, which counteracts the possibility of extinction of

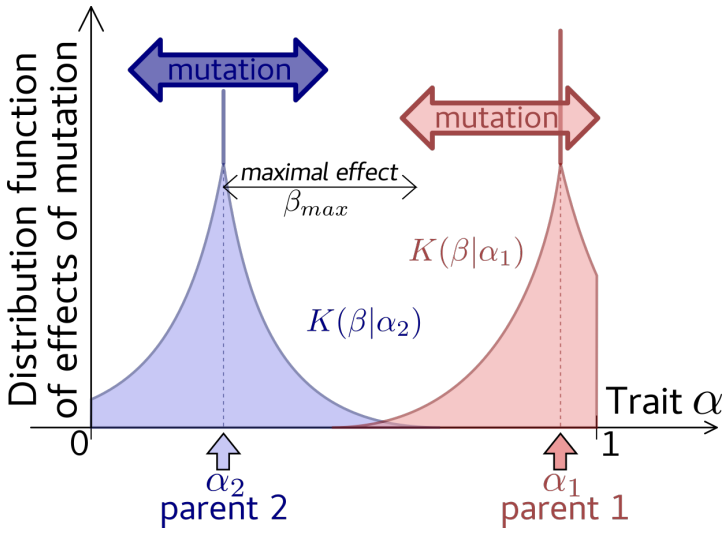


Figure 3: A3 – Distribution of mutational effects $K(\beta|\alpha)$. Each parent of trait, e.g. α_1 or α_2, produce offspring with trait $\alpha_i + \beta$ where β has the density $K(\beta|\alpha_i)$ depending on its parent traits (red and blue curves for α_1 and α_2, respectively).

the whole population. This might be worth discussing as extinction might sometimes happen before the transition to mutualism.

Response: Our aim in using a binomial distribution as a stochastic bonus was to introduce variability into the fecundities. But as suggested using a Poisson distribution would introduce more variability and with a simpler methodology. We have modified our algorithm in this sense, and this does not change the results of the model. We add the following sentence in the Methods and in appendix A.1:

line 162 page 4:

" Each agent produces offspring according to a Poisson distribution with parameter f, which corresponds to its fecundity. The fecundity defines the average number of offspring per agent. "

line 633 page 16:

"In general, the average offspring number f is not integer, yet the number of offspring in our model can only be represented by an integer. Thus, in the numerical algorithm, the fecundity was used as the λ parameter of a Poisson distribution. If the value drawn from the distribution was greater than the maximum fecundity f_{max}, then it was set back to the maximum fecundity."

1.5 Definitions and context

The introduction probably lacks a little bit of definitions/context:

* as noted by one of the referees, I guess you should use "joint evolution" instead of "coevolution" when you refer to the evolution of different traits in the same species

Response: Done

* the definition of symbiosis you use is not completely consensual – some people still understand symbiosis as mutualistic symbiosis. For this reason, I encourage you to write your definition early in the introduction.

Response: We added the following footnote on *page 1*:

"Symbiosis is used here in its etymological sense of "living together", encompassing parasitic and mutualistic symbiosis."

* since you use a parallel with altruism, I guess you also need to explicit what is altruism and how you distinguish mutualism from altruism.

Response: We added the following footnote on *page 2*:

"An altruistic trait benefits conspecifics, at a cost to its bearer. In contrast, a mutualistic trait benefits heterospecifics."

1.6 Symbiosis background

As you tackle the evolution of symbiotic entities, some background on symbiosis as an evolutionary force would help, e.g. Margulis and Sagan (2002).

Response: We added the following sentence

line 29 page 1:

"Egalitarian transitions are generally achieved through mutualistic symbiosis between a relatively large host and its symbiont and constitute one of the main sources of new lineages, underlying the origin of the eucaryotic cell and photosynthetic eucaryotes for instance [Margulis and Sagan, 2002]"

1.7 Interactors/replicators

The notions of interactors and replicators of Hull (1980) are also interesting in your context,

Response: We addressed this issue in the discussion, section "The interplay between several levels of selection"

1.8 Holobiont

as well as the more recent idea of the holobiont (e.g. Bordenstein and Theis 2015; Doolittle and Booth 2017).

Response: Yes, we established this connection adding the following:

line 32 page 1: "In many cases symbionts are microbes which are hosted by large eucaryotes, the whole corresponding to a holobiont [Gilbert et al., 2012, Bordenstein and Theis, 2015]"

I saw you referred to Sachs et al. (2011), maybe you could give the transition counts they put in their Fig. 3 to illustrate the importance of mutualistic transitions?

Response: The counts they put in Fig. 3 seem to advocate that parasitism evolves more likely than mutualism. We therefore added in the introduction:

line 88 page 2:

"In the case of holobionts, starting from free living bacteria Sachs et al. [2011] documented 27 transitions towards parasitism, 9 directly towards mutualism and 3 towards commensalism, whereas the transition from parasitism to mutualism occurred only 3 times. This highlights that the transition from parasitism to mutualism, although feasible, is relatively infrequent, and calls for a theoretical understanding of the mechanisms involved."

1.9 Red Queen

Because your initial state is one of parasitism, I found it bizarre that there is no mention of Red Queen dynamics in your introduction or discussion. For instance, would you expect the same speed of transitions if both hosts and symbionts had alleles that should match for the parasite to infect the host (or reciprocally for the host to be defended against the parasite)? It would probably be better if you could discuss a little what you think would happen in your model if either parasites and hosts were differentially locally adapted (as in the matching allele paradigm) or if parasites and hosts sequentially gained adaptations to counter the effect of the other (as in the gene-for-gene paradigm). In Sasaki et al. (2002), the effect of migration in a spatially explicit Red Queen dynamics model is studied and the authors conclude that migration is a "cheap alternative" to sex in Red Queen dynamics – since your model includes dispersal but not sex, you might want to use this study as a benchmark for discussion.

Response: We added the following lines in the discussion:

line 448 page 13:

"The evolutionary dynamics of the parasitic system have been ignored here, although they might affect the probability of transition. In the model the hosts cannot become resistant against the parasitic symbiont, which fits with the "superpathogen" of the gene-for-gene model [Salathé et al., 2008]. This can be interpreted as a monomorphic long-term result of Red Queen dynamics, some constrain preventing the appearance of new resistant and virulent alleles. However, if the host-parasite interaction is instead ruled by a matching allele model [Salathé et al., 2008], dispersal and the associated spatial structure is likely to maintain polymorphism [Sasaki et al., 2002]. During the early stages of the transition, formerly

parasitic symbionts turned mutualistic will inherit this matching genetic system and will need to find compatible hosts. This adds another requirement, rendering the transition less likely."

1.10 Levels of selection

Since you introduce and compare some of your results with those known in the evolution of altruism, I guess you could make the distinction between results due to kin vs. group selection. Group selection has had a bad press for some time, but modern models are able to incorporate both group and kin selections (e.g. Simon et al. 2013).

Response: We addressed this issue in the discussion, section "The interplay between several levels of selection"

1.11 Short vs long-distance dispersal

In your model, the existence of clusters of mutualists is due to philopatry and increased fecundity, which leads to increased competition. However, if dispersal becomes local also for symbionts, these might suffer from a lack of percolation of cells in the grid (if host-occupied cells are not adjacent, a philopatric symbiont might not be able to "jump" over gaps in the host population). For a model dealing with the ecological considerations associated with local vs. global dispersal, see Huth et al. (2015).

Response: This was partly addressed in the section "The role of quasi-vertical transmission" in the discussion. We have added the following :

line 401 page 12: "As well as hosts, mutualistic symbionts may also suffer from limited dispersal when they need to percolate in a landscape of non-adjacent hosts, which explains why they maintain $\sim$ 20% of global dispersal (Figure 3). On the other hand, parasitic symbionts also evolve towards an intermediate dispersal strategy, although they tend to disperse globally much more often ($\sim$ 80%, Figure 3). In purely parasitic systems it has been shown that some degree of vertical transmission, which is close to local dispersal in our case, is necessary for persistence in fragmented landscapes [Su et al., 2019, Schinazi, 2000]. In those cases as well as here, the parasitic population needs some degree of local dispersal in order to exploit a patch of hosts, once it has been "found" by global dispersers. Intermediate dispersal strategies have been found to favor persistence of a variety of systems. For instance, frequent short-distance and rare long-distance dispersal together favor metacommunity persistence in fragmented habitats [Huth et al., 2015] and intermediate migration rate is required for the spread of cooperative strategies in spatial prisoner's dilemma games [Vainstein et al., 2007a]."

1.12 Type of mutualistic benefit

At the end of the introduction, I was left with a big question: in your model, we don't know what exactly is understood by mutualistic effort. Since mutualism can take many forms, it would be useful if you could specify whether you think your model fits exchanges of resources more than shared immunity or anti-predator behaviours or other types of mutualisms involving symbionts.

Response: We added the following at the end of the introduction :

line 143 page 3:
"The mutualistic effort encompass the provision of resources, shelter, immunity, anti-predator behaviours, digestive enzymes or any other type of benefit provided that this occurs at some cost."

1.13 Codes sharing

Regarding the simulations, as noted by all referees, it would be nice to have the code somewhere accessible. Also, if you could give more details regarding simulations (duration, number of replicates per run, all tested parameter values, size of the grid, torus or absorbing boundaries or reflecting boundaries?), this would be invaluable.

Response: All codes are available on a public github repository:
`https://github.com/leoledru/PCI-Ledru-et-al.-2021-`

We add the following section at the end of our manuscript

line 598 page 16
"**Data and code accessibility**

All the codes used to compute the outcomes of our model and the figures of the paper are available on the following github repository: `https://github.com/leoledru/PCI-Ledru-et-al.-2021-`.

1.14 Measure of spatial autocorrelation

In terms of statistics to present your simulation outputs, you use an assortment index which I did not understand – can you write down its formula please? Also, why don't you give simpler things like Moran index of hosts and symbionts, join count statistics, spatial autocorrelation statistics, etc. ? Computing the population growth rate (using Euler-Lotka or something similar) and plotting that in relation to e.g. competition strength might also help.

Response: Our first idea was to compare locally the interaction trait of individuals with the interaction trait of their neighbors. We used an assortment index based on the distance between the traits. For each simulation and time t, we compute the similarity indices S_h and S_s respectively among hosts and symbionts, as follows

$$S_h(t) = 1 - \frac{1}{N_h} \sum_h |\alpha_h - \overline{\alpha}_h| \tag{3}$$

where α_h is the trait of the host h and N_h is the total number of host in the landscape at time t. The quantity $\overline{\alpha}_h$ is the mean trait in the neighborhood V_h of the host h (V_h is the 8 closest cell surrounding the host h). It is defined by

$$\overline{\alpha}_h = \frac{1}{|V_h|} \sum_{i \in V_h} \alpha_i.$$

The index for symbionts is computed similarly.

We build the assortment index A_h as the difference between the similarity index of host S_h observed and the similarity index S_{rh} of host when we randomly assigned trait of the host over the landscape,

$$A_h(t) = S_h(t) - S_{rh}(t). \tag{4}$$

Our index is different from the Moran index I which is defined with our notations by

$$I = \frac{N_h}{\sum_h |V_h|} \frac{\sum_h |V_h|(\alpha_h - \overline{\alpha})(\overline{\alpha}_h - \overline{\alpha})}{\sum_h (\alpha_h - \overline{\alpha})^2} \quad \text{and} \quad \overline{\alpha} = \frac{1}{N_h} \sum_h \alpha_h. \tag{5}$$

We also compute the Moran index for the host and symbiont. Our assortment and the Moran index show the same pattern. A positive spatial autocorrelation is observed after the transition occurred (see Fig.A4).

For the assortment index between host and symbiont, we also use a measure of similarity between the host and symbiont trait at each location of the couple. More precisely, we define for each simulation and each time t the similarity index S_{sh} between host and symbiont sharing the same location as follows

$$S_{sh}(t) = 1 - \frac{1}{N_s} \sum_s |\alpha_s - \alpha_h| \tag{6}$$

where N_s is the number of symbiont, which is also the number of host–symbiont couple. As before, we compare this observed index with the random index S_{rsh} defined by randomly rearranging pairs of symbiont and host. The assortment index A_{sh} is thus given by

$$A_{sh}(t) = S_{sh}(t) - S_{rsh}(t). \tag{7}$$

We also compare our index with the correlation coefficient between the interaction traits of hosts and symbionts. We find a positive correlation between trait in a same location (see Fig.A4).

As a conclusion, we clarify our approach by adding the section "Assortment index" in the appendix A.2. and we rewrite the section "Assortment index" in the methods section:

line 213 page 6:

"To investigate the spatial structure, which comes along with the transition to mutualism, we compute assortment indices: intraspesific indices measuring the spatial autocorrelation among hosts and symbionts and an interspecific index quantifying the correlation between phenotypes of host and symbiont sharing

the same location. More specifically, the intraspecific indices compute the similarity between the trait of an organism and the traits of its neighbors located in the 8 cells around it, and compare it with the similarity between the organismic trait and the mean trait over the landscape (details in appendix A.1). If the intraspecific index is positive (respectively negative), it means that on average the neighbors of any organism share similar (respectively dissimilar) traits. Similarly, the interspecific index is positive if hosts and symbionts sharing the same cell have similar interaction traits. Spatial aggregation indices for hosts, mutualistic symbionts and parasitic symbionts were also computed, measuring the formation of clusters (appendix A.1 for details)."

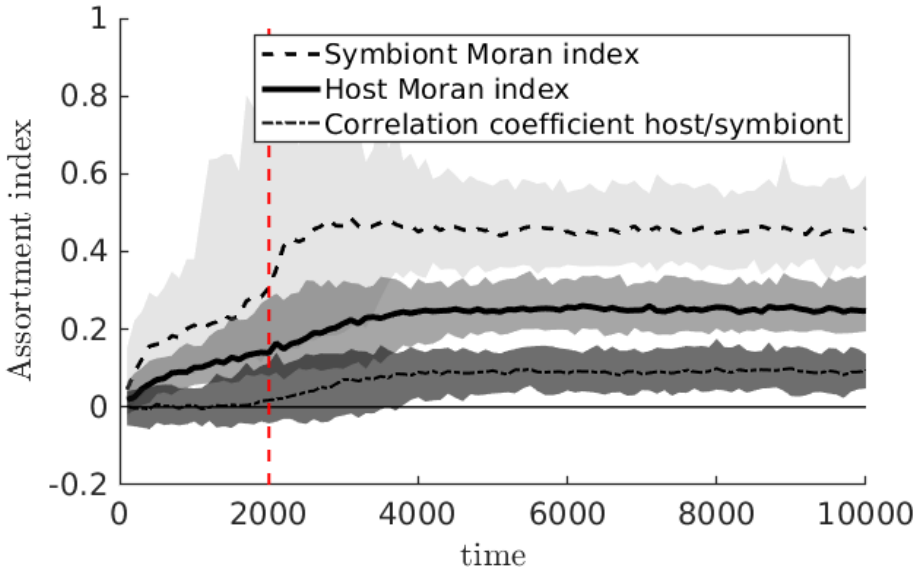


Figure 4: A6 – Spatial autocorrelation among hosts (plain curve) and symbionts (dashed curve) are described by the Moran index. The spatial correlation between the host and symbionts are described by the correlation coefficient (dash-dotted curve). The shadow regions corresponds to the interval at 5% and curves corresponds to the median over 100 replicates. The parameters are similar as Fig. 4.

1.15 Text clarity

As some of the referees remarked, you can still improve the clarity of the text. Some sentences (especially at the end of the introduction and in the discussion) should be rewritten.

Response: We have re-written large parts of the manuscript, paying attention to the clarity of the text.

1.16 Bibliography errors

Regarding presentation and formatting, my biggest remark would be to check thoroughly the names of authors in the references and when cited in the text: it looks like your bibliography is not very fond of authors with two surnames without hyphens, like the poor John MAYNARD SMITH who appears sometimes as Smith, sometimes as Maynard... Some other authors might have received the same treatment (I only saw Minus VAN BAALEN who lost his VAN, but others might have been injured too), so please pay attention and revise your .bib accordingly.

Response: Done

1.17 Coherence of mathematical notations

Another presentation/clarity item stems from the mathematical notations: some symbols (like c) are used to note very different quantities. My suggestion is to use other letters – use a different letter for each different quantities. Also, as remarked by referees, please try to stay consistent in the way you write parameters (superscript vs. subscript, etc.).

Response: The mathematical notations have been revised to be consistent.

1.18 Appendix

It is quite frustrating not to have a more thorough explanation of the model in the main text – can you please move some of the content from appendix A to the model and methods? Also, if you could add all parameters in the associated table, so that readers can refer to the table and find the interpretation of each parameter easily, that would be really nice.

To clarify, the mathematical background of our model we add some details in the "Methods" section. In particular, we introduce all the parameters and we provide a Table A1 in appendix, with all these parameters with their current value. In the table with also add a range of value that has been tested.

- **Fecundity and mutualism/parasitism.** We include the following additional information

line 162 page 4: "Each agent produces offspring according to a Poisson distribution with parameter f, which corresponds to its fecundity. The fecundity defines the average number of offspring per agent. It results from an interaction fecundity positively dependent on the trait of its cell-sharing partner and a mutualistic cost negatively dependent on its trait.

Specifically, the fecundity of a symbiont f^s of trait α_s in interaction with a host of trait α_h is defined by:

$$f^s(\alpha_s, \alpha_h) = (1 - c_m\,\alpha_s)\big(f^s_{min} + (f_{max} - f^s_{min})\alpha_h\big) \tag{8}$$

where c_m is the maximal mutualistic cost and f^s_{min} and f_{max} are the minimal and maximal interaction fecundity of symbionts. Similarly, the fecundity of a host f^h of trait α_h in interaction with a symbiont of trait α_s is defined by:

$$f^h(\alpha_h, \alpha_s) = (1 - c_m\,\alpha_h)\big(f^h_{min} + (f_{max} - f^h_{min})\alpha_s^{\gamma_f}\big) \tag{9}$$

where f^h_{min} is the minimal interaction fecundity of hosts and γ_f describes the selection strength on the trait α_s – the selection strength on α_h is set to $\gamma_s = 1$.

Since hosts are autonomous, in absence of symbionts, their fecundity f^{ha} only depends on their trait α_h:

$$f^{ha}(\alpha_h) = (1 - c_m\,\alpha_h) f^a \tag{10}$$

where the fecundity alone f^a ranges between the minimal and maximal interaction fecundity: $f^h_{min} < f^a < f_{max}$. As a result, the establishment of a symbiont with a low interaction trait ($\alpha_s < \alpha^*_s$) reduces the fecundity of the host; the symbiont is parasitic. Instead, a symbiont with a large interaction trait ($\alpha_s > \alpha^*_s$) enhances the host's fecundity; the symbiont is mutualistic. The threshold α^*_s is defined by $f^h(\alpha_h, \alpha^*_s) = f^{ha}(\alpha_h)$ (see appendix A.1 for mathematical derivation of the threshold). In the simulations, $\alpha^*_s = 0.475$ (Figure 1)."

- **Mutation.** We add a figure in appendix, which explain the process:

line 173 page 4:

"Offspring inherit traits from their parents with variability due to mutations. The effects of mutations on each trait are independent . However, the distribution of mutation effects does depend on the background phenotype, through its trait. We use a Beta distribution with shape parameters $(1, 3)$ to describe the amplitude of these effects, which could be either beneficial or detrimental. This mutation kernel allows for rare mutations with large effects. However, these effects can not exceed a maximal mutation size set to $\beta_{max} = 0.5$ (see Fig. A3 in appendix A.1 for details)."

- **Dispersal.** We provide a new figure in appendix to explain the dispersal process.

line 180 page 4

" ... (see Fig. A5 for a sketch of the process). "

- **Parasitic system and transition.** We justify the parameters range for the viabilty of the parasitic system based on the new appendix A.2 on the mathematical approximations. Moreover, we justify the 10% threshold using our mathematical approximation and a new Fig.A9 showing the % of mutualistic symbionts over time for different simulations.

line 195 page 5:

"To tackle the issue of transition to mutualism, we assume that the system is viable without mutualism (see appendix A.2 for details). More precisely, in the absence of mutation, the extinction probability of a population with parasitic global dispersers without dispersal cost (minimal interaction traits, $\alpha_s = \alpha_h = 0$, dispersal trait $\varepsilon = 1$ and dispersal cost $d = 0$) is given by $m/\big((1-m)f^a\big)$ where m is the mortality rate and f^a the fecundity of a parasitic host without symbiont.. We choose parameters such that the extinction probability is less than 1. In this case, the population stabilizes around a demographic equilibrium called the "parasitic system" where host density is around 0.15 and the symbiont density is around 0.1 with parameters value set in Table 1 (see Figure 2b-c and appendix A.2). From our perspective, this situation is the worst-case scenario because interactions are parasitic and dispersal cost is minimal. Then, mutualistic symbionts can appear by mutation, which generates approximately 2% of mutualistic symbionts in the population (see dashed purple curve in Figure 2c and Figure A8d). Natural selection eventually leads to a significant increase of the percentage of mutualistic symbionts, far above the 2% generated by mutations (Figure 2). Using an approximation model, we show that the extinction probability of mutualistic symbionts falls below 1 when the percentage of symbiont rises above 10% (appendix A.2 for details). In the simulations, a high density of mutualistic symbionts indeed persists in the long term when the percentage of mutualistic symbionts stands above 10% (Figure A9), which therefore characterizes the transition to mutualism. The transition time was defined as the time at which the percentage of mutualistic symbionts rises above this threshold."

• **Assortment indices and aggregation index.** We reformulate this paragraph but we put the formula in appendix for the fluidity of the text. We also compare our assortment index with more classical indes (Moran index and autocorrelation coefficient see Fig.A6). We also add an aggregation index, which only focus on spatial structure(see Fig.A7).

line 213 page 6:

" To investigate the spatial structure, which comes along with the transition to mutualism, we compute assortment indices: intraspesific indices measuring the spatial autocorrelation among hosts and symbionts and an interspecific index quantifying the correlation between phenotypes of host and symbiont sharing the same location. More specifically, the intraspecific indices compute the similarity between the trait of an organism and the traits of its neighbors located in the 8 cells around it, and compare it with the similarity between the organismic trait and the mean trait over the landscape (details in appendix A.1). If the intraspecific index is positive (respectively negative), it means that on average the neighbors of any organism share similar (respectively dissimilar) traits. Similarly, the interspecific index is positive if hosts and symbionts sharing the same cell have similar interaction traits. Spatial aggregation indices for hosts, mutualistic symbionts and parasitic symbionts were also computed, measuring the formation of clusters (appendix A.1 for details)."

1.19 Add all parameters used in captions of figures

A final remark: please pay attention to give all parameter values under plots if their values are not given by default in the summary table. For instance c_s is never given.

Response: The captions of the figures have been revised to give all the parameters used for the simulations.

2 Reviewer 2

2.1 General comments

The preprint by Ledru et al. "Mutualists construct the ecological conditions that trigger the transition from parasitism" investigates the transition from parasitism to mutualism that can be predicted to happen in the long term when parasites are closely associated (e.g. via vertical transmission) with their host. The interesting point explored in the preprint is that the spatial context may matter: dispersal evolution towards short-distance dispersal may kickstart the transition from parasitism to mutualism even when transmission is not strictly vertical. The manuscript reads very nicely and I read it with great interest. Please find some general as well as some more details comments below.

2.2 Link to prisoners' dilemma work

Introduction: I would suggest to discuss a little more in detail the mechanisms of repeated interactions vs. relatedness. This would allow to link to classical prisoners' dilemma work.

Response: We have added in the discussion a paragraph ("Benefits and costs") tackling these issues. We have also added in the discussion a citation of Vainstein et al. [2007b], who found that an "intermediate migration rate is required for the spread of cooperative strategies in spatial prisoner's dilemma games".

line 434 page 13:

"Benefits and costs. Benefits only depend on the interaction trait of the partner. In turn, costs depend on the interaction trait of the focal organism as well as on the benefits provided by the partner (Appendix A.1). This would correspond for instance to the development of organs like plant domatia [Szilágyi et al., 2009]: if the symbiotic ants are mutualistic, the plant can grow bigger, thereby producing more domatia, which is more costly in absolute terms. An alternative would be to assume that the costs do not increase with the mutualistic benefit; this would in any case be favourable to the evolution of mutualism. Moreover, in the model some cost is paid even if the partner is parasitic or if the host is free of symbiont. For instance, domatia or extrafloral nectaries are unconditionally produced [Bronstein, 1998], even though domatia size can be plastic [Kokolo et al., 2020]. Also, plants produce costly floral displays even in the absence of pollinators. Finally, another alternative arises when partners interact repeatedly, for instance during their growth. Using an iterated prisoners' dilemma model, Doebeli and Knowlton [1998] assumed that large received benefits trigger higher investment in the relationship. The interaction traits therefore become subject to phenotypic plasticity, in function of the partner's trait. This assumption favors the transition to mutualism since mutualists benefit more from being associated with mutualists. In contrast, our set of assumptions is more conservative."

2.3 Kin interactions

For readers who are not familiar with individual-based models it may be useful to more explicitly discuss kin interactions in the model and why the model includes this (e.g., Poethke et al. 2007 Ecol. Evol. Res.).

Response: Following this comment and comment 1.10 as well, we have now discussed in detail the kin selection and the multilevel selection. Please see section "The interplay between several levels of selection" in the discussion *(line 490 page 14)*.

We have also added in the discussion :

line 412 page 12: "This is in line with [...] the evolution of dispersal which is in part due to the reduction of kin competition [Hamilton and May, 1977, Poethke et al., 2007]"

2.4 Literature of horizontal vs. vertical transmission in parasitic systems

In addition, some more literature and discussion on horizontal vs. vertical transmission could be beneficial, such as Schinazi (2000) Math. Biosci., Saikkonen et al. 2002 PRSB, Su et al. (2018) Physica A, just as a few examples.

Response: We modified the following sentence in the introduction:

line 46 page 2:

"As a result, vertical transmission of symbionts promotes the transition to mutualism [Smith, 1998, Herre et al., 1999, Wilkinson and Sherratt, 2001, Ferdy and Godelle, 2005, Kerr and Nahum, 2011, Akçay, 2015, Estrela et al., 2016, Queller and Strassmann, 2016, Doebeli and Knowlton, 1998], although symbionts vertically transmitted can persist without becoming mutualists [Saikkonen et al., 2002]."

And we added the following in the discussion:

line 403 page 12:

"On the other hand, parasitic symbionts also evolve towards in intermediate dispersal strategy, although they tend to disperse globally much more often ($\sim 80\%$, Figure 3). In purely parasitic systems, it has been shown that some degree of vertical transmission, which is close to local dispersal in our case, is necessary for persistence in fragmented landscapes, because [Su et al., 2019, Schinazi, 2000]. In those

cases as well as here, the parasitic population needs some degree of local dispersal in order to exploit a patch of hosts, once it has been "found" by global dispersers."

2.5 Codes sharing

Finally, I would like to encourage the authors to publish the code of their simulations for the sake of reproducibility. Github and Zenodo, for example, allow to generate DOIs very easily.

Response : This was also suggested in comment 1.13. All codes are available on a public github repository:
https://github.com/leoledru/PCI-Ledru-et-al.-2021-

2.6 Coevolution

Wording: I am wondering whether "coevolution" of mutualism and dispersal (throughout the manuscript) is the right term. I would have suggested "concurrent" evolution.

Response: This point was also raised in section 1.5. Please refer to our response there.

2.7 Mutation model

Mutation procedure - exponential distribution. A lot of individual-based models follow a "classical" assumption of normal distributions for mutations. Could the authors justify their choice of the exponential a little more and maybe even test whether this assumption impacts their results?

Response : The use of an exponential distribution allows us to consider rare large mutations. Indeed, our model with a continuous interaction trait (rather than a binary parasitic/mutualistic trait) corresponds to a difficult situation for the emergence of mutualism since it often does not take a single mutation for a parasitic organism to see its offspring being mutualistic. However, the inclusion of large mutations, although rare, increases the probability of having a mutualistic offspring from a parasitic parent. Thus, mutation size may indeed play a role in the probability of transition, as shown in Figure A4 (not shown in the manuscript).

Moreover, following the suggestion 1.3 the model now uses a beta distribution in order to have a distribution bounded between 0 and 1. So, please refer to comment 1.3 for an explanation of our new choice, which induced the following modification in the main text and the additional section "Distribution of mutation effects" in the appendix A.2 (line 644 page 18):

line 173 page 4

"Offspring inherit traits from their parents with variability due to mutations. The effects of mutations on each trait are independent . However, the distribution of mutation effects does depend on the trait of the parents. We use a Beta distribution with shape parameters $(1, 3)$ to describe the amplitude of these effects, which could be either beneficial or detrimental. This mutation kernel allows for rare mutations with large effects. However, these effects can not exceed a maximal mutation size set to $\beta_{max} = 0.5$ (see Figure A3 in appendix A.1 for details)."

2.8 Parameters table and sensitivity analysis

Sensitivity analysis / Tab A1: some of the parameters have been tested systematically (e.g., mortality) but other do not seem to have been tested. Please update the table with all tested values and perform a sensitivity analysis on the parameters that have not been varied, where appropriate.

Response : The table 1 has been completed with the ranges of values used for the sensitivity analyses (see Table 1).

However, we did not perform a sensitivity analysis with respect to all the fecundity parameters but we investigate their role through the mathematical analysis of the approximation models (see appendix A.2 "Mathematical approximations" on page 22–24). In particular these analysis allows to choose these parameters such that parasitic system is viable and the host alone is viable.

2.9 Transition threshold of 10%

Transition threshold of 10%. The choice looks OK from Fig. 2 but slightly more justification in the text would help the reader understand the consequences of this choice. A sensitivity analysis may also be appropriate.

Parameters		Reference values	Sensitivity analysis range
m	probability of mortality	0.06	$[0.005; 0.15]$
c_m	maximum mutualistic cost	0.3	$[0; 1]$
f_{max}	maximal host and symbiont interaction fecundity	8	fixed
f^h_{min}	minimal host interaction fecundity	0.1	fixed
f^s_{min}	minimal symbiont interaction fecundity	2.5	fixed
f^a	maximal solitary host fecundity	0.5	fixed
γ_f	selection strength on the symbiont interaction trait	4	fixed
β_{max}	maximum mutation size	0.5	$[0.1; 1]$
w_h	scale of host competition	1	0 or 1
γ_c	strength of host competition	0.2	$[0.1; 2]$
d	dispersal cost	0	$[0; 1]$

Table 1: List of parameters and their reference values used for the simulations. The parameters of host and symbiont fecundities are determined to ensure the viability of the antagonistic system, therefore they are fixed because they are constitutive of the model.

Response: To clarify the choice of this threshold, we first show using our simulation outputs that the percentage of mutualistic symbionts either remains close to 2% or rises above 10% and stabilizes around 12.5% (see Fig.A9 in appendix A.2). In addition, we use simple deterministic model to justify this choice. From our mathematical model developed in appendix A.2, we are able to compute the extinction probability of the mutualistic symbiont (see section "Transition from parasitic system to mutualistic/parasitic system" in Appendix A.2.) We show that this probability falls below 1 if the percentage of mutualistic symbionts rises above 10%. We explain this in the methods section of our paper:

line 203 page 5:
"Then, mutualistic symbionts can appear by mutation, which generates approximately 2% of mutualistic symbionts in the population (see dashed purple curve in Figure 2c and Figure A8d). Natural selection eventually leads to a significant increase of the percentage of mutualistic symbionts, far above the 2% generated by mutations (Figure 2). Using an approximation model, we show that the extinction probability of mutualistic symbionts falls below 1 when the percentage of symbiont rises above 10% (appendix A.2 for details). In the simulations, a high density of mutualistic symbionts indeed persists in the long term when the percentage of mutualistic symbionts stands above 10% (Figure A9), which therefore characterizes the transition to mutualism. The transition time was defined as the time at which the percentage of mutualistic symbionts rises above this threshold."

2.10 p-values

Fig 3b: The correlation is fine, but stats with p-values don't make a lot of sense on simulated data. Please delete the p-values.

Response: We delete the p-value.

3 Reviewer 3

3.1 General comments

I found this paper interesting, especially the role of competition in the evolution of mutualism and the fact that it happens best on the edge of viability (Figure 6). This was unexpected to me and so the paper changed the way I think about the evolution of mutualism in spatial systems. I am happy to recommend accepting this paper after revisions.

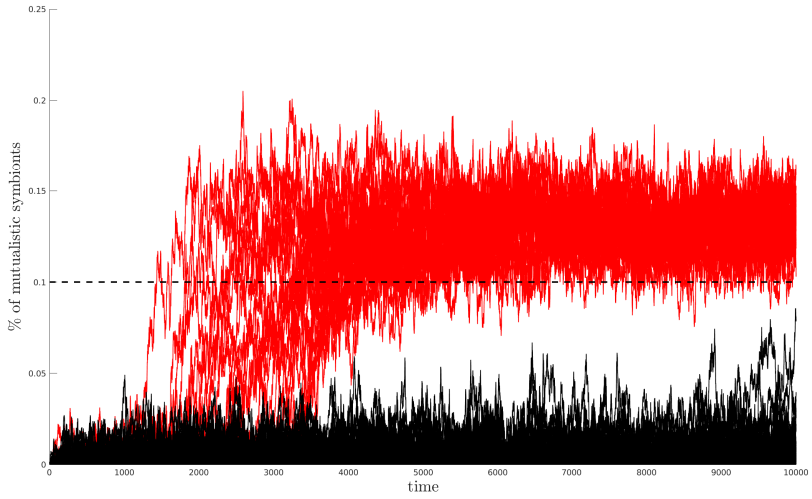


Figure 5: A9 – Evolution of the percentage of mutualistic symbionts in the population over 129 simulations. Red curves corresponds to replicates such that the percentage of mutualistic symbionts remains greater than the threshold of 10% – transition to mutualism. Black curves corresponds to replicates where the percentage remains below the 10% threshold – no transition.

3.2 Dispersal cost 1

What I expected to see is the following scenario: First dispersal evolves to be local due to the cost of global dispersal; and once this has happened, the resulting kinship structure selects for mutualism. After reading the paper, I still think that this is an important route to mutualism and this explains why mutualism evolves in 100% of simulations and within a short time when dispersal is costly (Figure 2a).

Response: We agree, this is the way mutualism evolves if dispersal is costly. However, since we also try to explain how mutualism evolves in the absence of dispersal cost, we are looking for another mechanism.

The paper shows that mutualistic symbionts indeed have local dispersal, but Figure 3 is only a snapshot; it would be interesting to know whether it is dispersal that first evolves to be local and mutualism evolves later. In this case, there is no need for multiple random events to happen at the same time (explaining why the transition is fast).

Response: Figure 3 corresponds to a simulation without dispersal cost, as specified in its legend. In that case, local dispersal and mutualism evolve simultaneously, and multiple random events must happen together for the initiation of the transition. We can observe this simultaneous emergence in Figure 6.

From my first reading of the paper, I got the impression that the authors consider the effect of dispersal cost to be analogous to the effect of mortality (both reduce density).

Response: The reduction of density does not favour mutualism, since intraspecific host competition is important for the transition. Instead, dispersal cost facilitates the transition to mutualism because it first triggers the evolution of local dispersal, as discussed above. Mortality does not have the same effect: when mortality is high, the parasitic system is close to its viability boundary (Figure 6). Therefore, the increase of host density following the transition to mutualism renders the parasitic system unviable more easily. This issue has now been included in the discussion:

line 359 page 11:

"**The impact of dispersal cost and mortality.** As expected, dispersal cost speeds up the transition (Figure 2a and 6) because it induces a selection pressure at the organismic level in favour with local dispersal, which increases the likelihood of the formation of mutualistic clusters. Mortality also enhances the probability of transition (Figure 6), but with another mechanism. We have stressed that competition between hosts creates an eco-evolutionary feedback loop, where the evolution of mutualism increases global densities, which strengthens competition and therefore turns the growth rate of the parasitic system negative. Given that mortality pushes the parasitic system towards its viability boundary, high mortality enhances the ability of competition to launch the transition. Although the

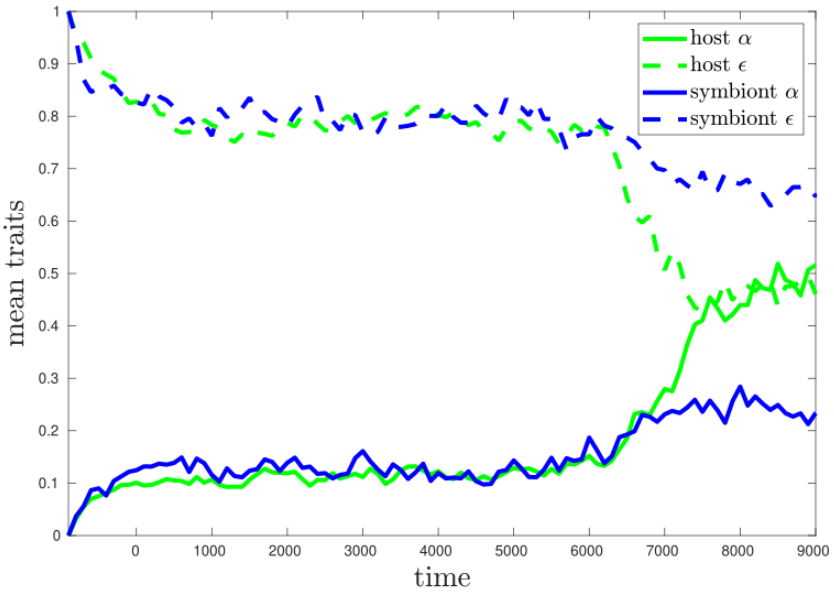


Figure 6: Evolution of the mean traits of hosts (green curves) and symbionts (blue curve) over time during a simulation leading to transition: dashed curves correspond to the dispersal traits of hosts ε_h and symbionts ε_s and plain curves correspond to the interaction traits of hosts α_h and symbionts α_s.

transition occurs in a wide range of parameters where the parasitic system is viable, it is more likely when the parasitic system is close to extinction (Figure 6). However, mortality cannot itself trigger the transition since the parasitic system is unviable from the start when mortality is too high. Finally, mortality may also facilitate the transition through the reduction of global densities, which decreases the threat of parasites invading mutualistic clusters. The facilitation of mutualistic symbiosis in harsh environmental conditions has also been observed in previous empirical [Callaway et al., 2002, Maestre et al., 2003, Werner et al., 2015] and theoretical [Travis et al., 2006] works. However in the context of altruism the opposite relationship was found [Taylor and Irwin, 2000]."

In contrast to this, I think that the cost directly selecting for local dispersal is instrumental in the evolution of mutualistic clusters.

Response: Yes it is. We have now specified it in the text:

line 235 page 6:
"Dispersal cost was therefore used as an instrumental tool to speed up the transition when necessary."

3.3 Mortality and competition 1

A main effect of competition is to reduce global density and hence the threat from invading parasites. The same effect should follow from increased mortality. Indeed, Figure 6 shows that increased mortality helps the evolution of mutualism, but the analogous effect to competition is not discussed. I think that strong competition is largely analogous to high mortality, with one difference: strong competition increases mortality (from failure of establishment) when mutualism evolves but not before, i.e., it allows for higher densities and therefore more mutations and simultaneous rare events at the beginning, perhaps shortening the time till mutualism appears.

Response: The effects of mortality and competition are indeed interwoven, but we do not think they are analogous. Please refer to our answer to comment 3.2 above.

3.4 Appendix

The paper is reasonably well written, but at several places, I had to consult the appendix to make out what the main text means. Since there is no limit on the length of the main text, I propose moving all essential details of the model to the main text. Readers not interested in formulas can easily skip over if

these specifications follow the current verbal description e.g. with the words "Specifically, we assume..." [and here the part moved from the Appendix follows].

Response: We add some formula in the main text to clarify the model and introduce all the parameters discussed in the "Results" section. Please see our response to comment 1.18 which details our changes in the "Methods" section of the main text.

3.5 Baseline without competition

It may be useful to include the results of a baseline simulation with no competition at all but otherwise favourable conditions for the evolution of mutualism (relatively high mortality to be near the edge of viability, with and without dispersal cost).

Response: Competition for space and more importantly the presence of parasites together regulate the population of hosts. The host population may also be limited by intraspecific competition for resources other than space, depending on the strength of host competition γ_C. When $\gamma_C = 2$, competition between hosts is negligible, because the densities reached by hosts are much below the densities at which competition would have produced any effect. The parameter value $\gamma_C = 2$ therefore corresponds to the baseline simulation, either with dispersal cost (Figure 5a) or without dispersal cost (Figure 5c, reversal). With dispersal cost (Figure 5a), negligible competition does not entirely prevent the transition, the % of mutualistic symbionts being just above 10%. Without dispersal cost, the negligible competition causes mutualism reversal. In the manuscript, we have now distinguished strong competition ($\gamma_C = 0.2$), weak competition ($\gamma_C = 1$) and negligible competition ($\gamma_C = 2$). The last term was added in appendix A.3:

line 765 page 24:

"we suddenly switched the competition strength to $\gamma_C = 2$, corresponding to negligible competition. We observed reversal of mutualism due to the proportion of mutualistic symbionts decreasing from 20% to less than 5% (Figure A10a) and e))."

3.6 Dispersal cost and mortality

It was not clear to me whether the same cost of dispersal applies to both host and symbiont. In reality, it could be that global dispersal is costly for one but not the other. The same applies to mortality (m); why is it the same?

Response: The dispersal cost does apply to both hosts and symbionts. The dispersal cost of an agent (host or symbiont) with dispersal trait ε is given by $1 - d\,s\varepsilon$ where d is the dispersal cost intensity. This parameter d is the same for hosts and symbionts. Thus the dispersal trait have the same influence on both agents. This assumption might be discussed as suggested by the reviewer. For instance, if we reduce the dispersal cost for the host, then host will be more spread over the landscape, which will increase parasitic symbiont density which disperse more globally than mutualistic symbionts. This situation is in between the case without dispersal cost and with equal dispersal cost described in Fig.2. Since transition may occur even without dispersal cost, we expect transition to occur when dispersal cost are dissimilar. However, we have shown that increasing dispersal cost will always enhance transition from parasitism to mutualism (see Fig.2a)).

We clarify this point in the paragraph "Dispersal" of the methods section

line 188 pages 5:

"we assumed a linear trade-off ... and d the dispersal cost intensity, which is the same for both hosts and symbionts."

We also assume that the mortality rate m is also identical for hosts and symbionts. As before, we can discuss this point. First of all, the symbiont cannot survive without host, so if the host dies the symbiont also dies. Thus the mortality rate of the symbiont is larger than the mortality rate of the host. In addition, we can show from our mathematical approximation model, that the mortality rate of the host has more influence on the stability of the system than the mortality of symbiont, which only defines the amount of symbiont in the system. Indeed, in the parasitic system without mutation, the host mortality rate has a great impact on its stability. If it is too large the system is not viable while the system is always viable when it is low independently of the mortality rate of the symbionts. The mortality rate of the symbiont only impacts the amount of symbiont at equilibrium but does not change the stability of this equilibrium. Thus the host mortality rate seems more important in the system. And

an increase of symbiont mortality will just slow down the transition because the density of symbiont will be lower.

To clarify this point we refer to the appendix A.2.

line 698 page 22:

"Even if hosts and symbiont does not share the same mortality rate m, the model holds true by multiplying the terms f_s by $(1 - m_s)$ the survival rate of symbionts instead of $(1 - m)$. We can check that the following qualitative properties holds true with a different mortality rate. However, it will modify the quantitative outcome of the model."

3.7 Harada 1999

Harada 1999 (J. Theor. Biol. 201: 171-187) investigated the evolution of dispersal under a cost to global dispersal, the same as the present model assumes; this would be a relevant citation.

Response: we included this citation in the model description as well as in the discussion.

3.8 Evolutionary branching

what is seen in Figure 2 is not evolutionary branching; judging from the colours, the mutualistic branch starts out with a trait value rather different from that of the parasite. Perhaps a large mutation is needed to initiate the evolution of mutualism. "Evolutionary branching" is reserved for gradual divergence through only small steps.

Response: We agree that "evolutionary branching" is generally used within the framework of Adaptive Dynamics, which assumes gradual evolution. However, we delete the paragraph mentioning this issue.

3.9 Evolution of mutualistic hosts

"Strong mutualistic hosts will benefit more from parasitic symbionts than weak mutualistic hosts. Indeed, a parasitic symbiont will benefit from a strong mutualistic host by increasing its number of offspring, which eventually reduces the host density and thus host competition." – this cannot select for host mutualism. The advantage of reduced host density is enjoyed by all hosts equally (non-mutualistic included) whereas the burden is on the mutualistic hosts. Therefore the latter is selected against.

Response: We agree that the above sentence, which has now been removed, could not explain selection for host mutualism. Instead, we have added the following paragraph in the discussion, and added the supplementary Figure 6.

line 382 page 12:

"**The evolution of mutualistic hosts.** So far, only the mechanisms responsible for the evolution of mutualistic symbionts have been elucidated, but not those involved in the evolution of mutualistic hosts. Surprisingly, mutualistic hosts evolve after the transition (Figure 2c). Following the transition, the density of mutualistic symbionts is much higher, so that mutualistic hosts tend to be associated with mutualistic symbionts (Figure 4c), which disperse locally (Figure 3a). In that case, mutualistic hosts will increase the local density of mutualistic symbionts in the following generations, which will benefit their offspring provided that they disperse locally as well (Figure 3b). Symbionts may become less abundant for instance because of additional intraspecific competition between them, as in Appendix A.5. As a result, more hosts remain non-mutualistic because they are less often associated with a symbiont (Figure A13), which further highlights that the evolution of mutualistic hosts relies on high symbiont densities."

3.10 Evolutionary rescue

Figure 6 shows evolution of mutualism outside the region where the ancestral parasitic system is viable: Is this a case of evolutionary rescue? How fast does it happen? In what percentage of simulations is rescue successful (i.e., the simulation does not die out)?

Response: Absolutely. We included two paragraphs in order to detail this interesting point.

In the results:

line 296 page 8:

"Finally, Figure 6 shows that for some parameter combination, mutualism evolves although the parasitic system is initially unviable. The viability of the parasitic system was assessed by simulations of

5000 time steps, without evolution. This implies that in a relatively short period of time in comparison to the waiting times shown in Figure 2 for other parameter values, transitions can occur quickly enough and prevent the extinction of a parasitic system otherwise unviable. However, this may occur rarely, Figure A14 shows that for some parameter combinations up to 90% of the simulations go extinct, the remaining being able to persist thanks to the evolution of mutualism. In those cases the mean percentage of mutualistic symbionts is much higher, ranging from 35 to 60%."

And in the discussion:

line 375 page 12:

"**Evolutionary rescue.** As evidenced by Figure 6, the evolution of mutualism can prevent the extinction of the parasitic system for parameter combinations that are just above the upper limit of the viability domain. This echoes the concept of evolutionary rescue [Ferriere and Legendre, 2013, Gomulkiewicz and Holt, 1995], according to which the persistence time of a population is longer with than without evolution. In the present case, instead of a single population, the populations of two distinct species are rescued by evolution. More generally, the parasitic system benefits from the evolution of mutualism even when it is initially viable, through an increase in population densities (Figure 2)."

3.11 Unclear sentence

"However, this only occurs when competition between hosts is partly global (Figure 5b); if it is purely local, mutualistic clusters cannot influence the viability of parasitic regions. Although areas dominated by parasitic host/symbiont pairs become unsuitable..." – I do not understand why these areas would become unsuitable; it seems to contradict the first sentence cited here.

Response: The two sentences should be read separately. We modified the sentence as follows:

line 343 page 11:

" However, this only occurs when competition between hosts is partly global (Figure 5b); if it is purely local, mutualistic clusters cannot influence the viability of parasitic regions and will suffer from kin competition. In line with hypothesis H4, local competition between hosts for resources thereby prevents the transition to mutualism. Local competition between hosts for available space also occurs when hosts disperse locally, but this does not jeopardize the transition."

3.12 Dispersal cost 2

"For this reason, the dispersal cost was introduced to speed up the transition (Figure 2a) without affecting the overall behaviour of the model. Dispersal cost induces a selection pressure at the individual level in favour of local dispersal, which increases the likelihood of the formation of mutualistic clusters." – I think the effect described in the second sentence is significant (see also above) and therefore the first sentence is incorrect in saying that the cost of dispersal has no important effect.

Response: This section was indeed unclear, those two sentences were not meant to work together and have therefore been separated. Furthermore, we have deleted "without affecting the overall behaviour of the model" in order to avoid confusion. We modified the text as follows:

line 359 page 11:

" As expected, dispersal cost speeds up the transition (Figure 2a and 6) because it induces a selection pressure at the organismic level in favour with local dispersal, which increases the likelihood of the formation of mutualistic clusters. Mortality also enhances the probability of transition (Figure 6), but with another mechanism."

3.13 Mortality and competition 2

"Mortality pushes the parasitic system towards its viability boundary and promotes the eco-evolutionary feedback loop involving host competition." – I think mortality does not promote the feedback through competition (and what does "promote" here mean?). As I argue before, mortality simply decreases density (akin to competition) and therefore decreases the threat of parasites invading mutualistic clusters.

Response: In our response to comment 3.2 above, we argue that mortality does promote the feedback through competition. We also acknowledge the possibility of a second mechanism, where mortality decreases the threat of parasites invading mutualistic clusters.

3.14 Cost of mutualism

By taking the product in equation 4 in the Appendix, the authors assume that individuals who get more help from their partner (high f_I) pay more for their own mutualism in absolute terms. It is unclear why this would be the case. The additive formula $f_h = f_{I,h} - c\alpha_h$ seems more appropriate. I suppose it would be too much work to run the simulations with additive cost, but this assumption should be discussed.

Response: A discussion of this topic has been added in the discussion, paragraph "Benefits and costs":

line 434 page 13:

" **Benefits and costs.** Benefits only depend on the interaction trait of the partner. In turn, costs depend on the interaction trait of the focal organism as well as on the benefits provided by the partner (Appendix A.1). This would correspond for instance to the development of organs like plant domatia [Szilágyi et al., 2009]: if the symbiotic ants are mutualistic, the plant can grow bigger, thereby producing more domatia, which is more costly in absolute terms. An alternative would be to assume that the costs do not increase with the mutualistic benefit; this would in any case be favourable to the evolution of mutualism. Moreover, in the model some cost is paid even if the partner is parasitic or if the host is free of symbiont. For instance, domatia or extrafloral nectaries are unconditionally produced [Bronstein, 1998], even though domatia size can be plastic [Kokolo et al., 2020]. Also, plants produce costly floral displays even in the absence of pollinators. Finally, another alternative arises when partners interact repeatedly, for instance during their growth. Using an iterated prisoners' dilemma model, Doebeli and Knowlton [1998] assumed that large received benefits trigger higher investment in the relationship. The interaction traits therefore become subject to phenotypic plasticity, in function of the partner's trait. This assumption favors the transition to mutualism since mutualists benefit more from being associated with mutualists. In contrast, our set of assumptions is more conservative."

3.15 Camille Noûs

The address of Nous is incomplete.

Response: Done

3.16 Global competition

On the first reading, it was not clear to me that equation 1 gives global competition (ρ_h could have been the proportion of neighbouring cells that are occupied; in a lattice model, a natural default assumption is that interactions are local).

We changed the equation 1 to clarify the difference between local and global competition, which clarifies the global density. We add the following sentence:

line 190 page 5:

"Hosts compete for empty cells, especially if they disperse locally. Beside space, hosts may also compete with each other for resources like water, light or food. In order to test hypothesis H3 we introduced intraspecific density-dependent competition, acting either at the local or the global scale. For instance, competition for light only involves the closest neighbors while competition for the water table might act at the entire space scale. The competition scale parameter w_h, ranging in $[0, 1]$, weights the effect of the local density ρ_h^{local} and the global density ρ_h^{global} of host on the competition. Competition reduces the establishment probability P_I of the offspring:

$$P_I = 1 - \left((1 - w_h)\rho_h^{local} + w_h\rho_h^{global}\right)^{\gamma_C} \tag{11}$$

The local host density ρ_h^{local} corresponds to the host density in the 8 neighbouring cells surrounding the offspring, while the global density ρ_h^{global} corresponds to the host density over the entire landscape (see Figure A2 for a schematic representation). The parameter γ_C corresponds to the competition strength. The competition is strong when $\gamma_C < 1$ (sub-linear function), while it is weak when $\gamma_C \geq 1$ (super-linear function)."

3.17 Transition threshold of 10%

"we assume that transition occurs when the percentage of mutualistic symbionts rises above the threshold of 10%" – a percentage relative to what?

We answer this issue in section 2.9. This threshold must be reached so that the extinction probability of the mutualistic symbionts falls below 1.

line 203 page 5:

"Then, mutualistic symbionts can appear by mutation, which generates approximately 2% of mutualistic symbionts in the population (see dashed purple curve in Figure 2c and Figure A8d). Natural selection eventually leads to a significant increase of the percentage of mutualistic symbionts, far above the 2% generated by mutations (Figure 2). Using an approximation model, we show that the extinction probability of mutualistic symbionts falls below 1 when the percentage of symbiont rises above 10% (appendix A.2 for details). In the simulations, a high density of mutualistic symbionts indeed persists in the long term when the percentage of mutualistic symbionts stands above 10% (Figure A9), which therefore characterizes the transition to mutualism. The transition time was defined as the time at which the percentage of mutualistic symbionts rises above this threshold."

3.18 Histogram of transition time

In Figure 2, it would be good to include a panel to show the probability of transition as a histogram (rather than just numbers in panel (a)). For more visual readers, what sticks from this figure is the small difference between the transition times when comparing weak and strong competition; the huge difference in transition success is overlooked.

Response: The figure has been modified accordingly: see Figure 2(a)

3.19 Unclear sentence

"Finally, we showed that mutualism persists only because of strong competition" – this is not so, Figure 2 does show counterexamples.

Response: We have modified the sentence to specify that it occurs only in the absence of dispersal cost:

line 267 page 6:

"In the absence of dispersal cost, when competition is reduced after the transition to mutualism, the system switches back to the parasitic state (Figure 5c, see Figure A10 for details)."

3.20 Strong competition

strong competition is sometimes referred to as "high" competition; this should be changed to "strong". (Even "strong" is somewhat a misnomer because it refers to the shape of the competition function rather than the magnitude.)

Response: We changed to "strong competition".

3.21 Perturbation explanation

the sentences pertaining to perturbation on page 8 are cryptic without consulting the Appendix

We clarify this point by explaining the perturbation in the text and adding the Fig.A4a in the main text. We also add in the figure the host density to see that perturbation means reduction of host density. We add the following sentence:

line 270 page 6:

"Another way to investigate the effect of competition is to reduce host density, through the eradication of hosts in a region after a transition to mutualism. At first, the perturbed region is mainly recolonized by hosts and parasitic symbionts (Figure A11b), but mutualistic symbionts persist in the landscape."

3.22 Legends

at the end of the legend of Fig 6, the text should probably refer to Fig 2, not Fig 3.

Response: Done

3.23 Clarification fecundity expressions

equation 2 in the Appendix is unnecessarily complicated: why do we divide with $f_{i,min}$ if we also multiply with it? It was also not clear to me why the minima differ but the same maximum applies to host and symbiont.

We modify the equation 2 in Appendix to clarify the fecundity. We choose the maximal fecundity $f_{max} = 8$ because when individuals disperse locally, it is the highest amount of offspring they could produce to fulfill the 8 local neighbors.

In the appendix we have now the following formula as well s in the main text

$$f_I^h(\alpha_s) = f_{min}^h + \left(f_{max} - f_{min}^h\right)\alpha_s^{\gamma_f}$$

$$f_I^s(\alpha_h) = f_{min}^s + \left(f_{max} - f_{min}^s\right)\alpha_h$$

3.24 Assortment index definition

In the section Assortment index in the Appendix, "difference" and "similarity" appear to be mixed up. It was not clear to me how the randomization is done: randomize symbionts over all hosts or over symbiont-bearing hosts?

We clarify the definition of the assortment by adding the mathematical formula associated to the indices in appendix A.1. The idea of our assortment index is first to measure a similarity index in our simulation outcomes and the same similarity index when we randomly redistributed traits among individuals with fixed location. In particular, for the intraspecific assortment index among host, at each time we keep the location of individuals the same but we redistributed the interaction traits randomly among the individuals and then we compute the similarity index. Then we compare those two similarity indices to compute the assortment indices. The specific computations and definitions of intraspecific and interspecific indices are given in the appendix A.1. Moreover, we compare our intraspecific assortment index with the classical Moran index and our interspecific assortment index with the correlation coefficient between host and symbionts sharing the same location.

In the main text we rewrite the section Assortment index:

line 213 page 6:

"**Assortment and aggregation indices.** To investigate the spatial structure, which comes along with the transition to mutualism, we compute assortment indices: intraspesific indices measuring the spatial autocorrelation among hosts and symbionts and an interspecific index quantifying the correlation between phenotypes of host and symbiont sharing the same location. More specifically, the intraspecific indices compute the similarity between the trait of an organism and the traits of its neighbors located in the 8 cells around it, and compare it with the similarity between the organismic trait and the mean trait over the landscape (details in appendix A.1). If the intraspecific index is positive (respectively negative), it means that on average the neighbors of any organism share similar (respectively dissimilar) traits. Similarly, the interspecific index is positive if hosts and symbionts sharing the same cell have similar interaction traits. Spatial aggregation indices for hosts, mutualistic symbionts and parasitic symbionts were also computed, measuring the formation of clusters (appendix A.1 for details)."

And we also add the following section in the appendix A.1

line 667 page 19:

"**Assortment index.** To compute the assortment index, we measured the similarity between spatially neighbouring phenotypes for the spacial repartition resulting from the transition to mutualism and for the same spacial repartition but with phenotypes randomly redistributed among individuals. The assortment index corresponds to the difference between the measurement made on the space resulting from the transition to mutualism and the measurement on the randomly rearranged space. If the index shifts positively (resp. negatively) from zero, it means that similar phenotypes are closer (resp. more distant) than different phenotypes compared to random spatial distribution. This methodology is similar to that used in Pepper and Smuts [2002] and Pepper [2007].

Intraspecific assortment index. More precisely, for the intraspecific assortment index we use the following similarity index for host and symbiont. For each simulation and time t, we compute the

similarity indices S_h and S_s respectively among hosts and symbionts, as follows

$$S_h(t) = 1 - \frac{1}{N_h} \sum_{h=1}^{N_h} |\alpha_h - \overline{\alpha}_h| \tag{12}$$

where α_h is the trait of the host h and N_h is the total number of host in the landscape at time t. The quantity $\overline{\alpha}_h$ is the average trait in the neighborhood V_h of the host h. The neighborhood V_h of a host h is the 8 closest cells surrounding it (figure A2). It is defined by

$$\overline{\alpha}_h = \frac{1}{|V_h|} \sum_{i \in V_h} \alpha_i.$$

The similarity index among symbionts S_s is computed similarly.

Then for each time, we reshuffle the traits among the location occupied by hosts and symbionts and we compute the associated similarity indices using equation (12). We average those indices over 1000 replicates to compute the similarity indice S_{rh} and S_{rs} corresponding to a random spatial distribution.

Finally, We build the assortment index A_h as the difference between the similarity index of host S_h observed and the similarity index S_{rh} of host when we randomly assigned trait of the host over the landscape,

$$A_h(t) = S_h(t) - S_{rh}(t). \tag{13}$$

We also compare our assortment index with the spatial autocorrelation Moran index for the host and symbiont. The two indices show the same pattern. A positive spatial autocorrelation is observed after the transition occurred (Figure A6).

Interspecific assortment index. For the assortment index between host and symbiont, we also use a measure of similarity between the host and symbiont trait at each location of the couple. More precisely, we define for each simulation and each time t the similarity index S_{sh} between host and symbiont sharing the same location as follows

$$S_{sh}(t) = 1 - \frac{1}{N_s} \sum_{s=1}^{N_s} |\alpha_s - \alpha_h| \tag{14}$$

where N_s is the number of symbiont, which is also the number of host–symbiont couple. As before, we compare this observed index with the random index S_{rsh} defined by randomly rearranging pairs of symbiont and host and taking average over 1000 replicates. The assortment index A_{sh} is thus given by

$$A_{sh}(t) = S_{sh}(t) - S_{rsh}(t). \tag{15}$$

We also compare our index with the correlation coefficient between the interaction traits of hosts and symbionts. We find a positive correlation between trait in a same location (Figure A6)."

4 Reviewer 4

4.1 General comments

The authors discuss in this manuscript an individual based model, investigating in a spatially explicit model how a symbiotic relationship between two species may have shifted from parasitism to mutualism. The presented questions are engaging, and well outlined in the introduction. The results are well structured and discussed (and I especially appreciate the clear and visually appealing figures). Below, I outline a number of comments, related to the presentation of the data and some of the model assumptions. However, I want to stress that overall, the manuscript was very well written, and I enjoyed reading it.

4.2 Expectations

Introduction: At the top of page 3, you have a very nice outline of the research questions, and you refer back to these original questions during the discussion. I very much appreciate this clear outline, however

I feel it would be even better to include along the questions your a priori hypotheses/expectations on what you expected related to these questions

Response: Since most of our expectations related to these questions were "Yes", we reformulated the sentences accordingly. Please refer to the corresponding section in the main text. We have also added two other hypothesis, following suggestion 5.2:

line 122 page 3:

- "**Main hypothesis:** In the absence of vertical transmission and partner control, we expect that the transition from parasitism to mutualism can occur when the mutualistic efforts of both hosts and symbionts jointly evolve with local dispersal.
- **H1:** The formation of mutualistic clusters should be necessary for the initiation of the transition. The emergence of spatial structure should come along with the transition.
- **H2:** By maintaining global dispersal, non-mutualistic hosts and parasitic symbionts should be able to coexist with mutualists.
- **H3:** The transition to mutualism is due to the relatively higher fecundity of mutualistic clusters.
- **H4:** If competition between hosts is mostly local, this should hamper the formation of mutualistic clusters, thereby preventing the transition.
- **H5:** We expect that mutualistic hosts will become ecologically dependent on their symbiont."

4.3 Joint dispersal

Model description: In many systems, dispersal of the parasite will be linked to the dispersal ability of the host. This simply because hosts tend to be larger and more capable of dispersal (e.g. birds displacing parasitic flatworms, ticks carried on large vertebrates). Whereas it is of course fine to make the assumption here that dispersal is independent for both interacting species, I feel it would nonetheless be important to discuss the reasoning behind this choice, perhaps link to an example in the natural world, and include in the discussion speculation on how this assumption may affect the outcome of the model. Especially because in such a case where dispersal of host and symbiont are dependent, even global dispersal may maintain more stronger clusters, as mutualist host and symbionts are likely to end up close to each other, even when they disperse further, maintaining spatial structure.

We agree with this idea. We included the following lines in the discussion:

line 426 page 13:

"**No vertical transmission.** We excluded the possibility of vertical transmission because it is a complex feature involving many traits, which more likely evolve some time after the transition once the mutualistic relationship is well established. For this reason an alternative mechanism is needed, and our results demonstrate that the coevolution of mutualistic effort and limited dispersal in both species can mimic vertical transmission, as argued above. However, in some parasitic systems (e.g. birds displacing parasitic flatworms, ticks carried on large vertebrates) vertical transmission may be a passive feature, present from the start. In such cases the evolution of mutualism is theoretically possible even if hosts keep dispersing globally, provided that mutations turning the parasites into mutualists exist."

4.4 Cost/benefit

Model description: Related to the cost/benefit of being associated with a host/ symbiont with a changing interaction trait (i.e. the relation shown in Figure 1). Both species seem to gain quite strong rewards for being associated when the interaction trait of the interacting species increases, yet you still find that typically only a small proportion of symbionts (up to about 20%; Figure 2C) becomes mutualistic. This made me wonder what would happen if you would alter the benefit function, would you still see a mutualistic strategy arising at all if the benefits are less strong? If such data exists on the simulation using a different benefit function, it may be useful to include in the appendix. If not, it may still be informative to discuss the expectations for changed benefits and how they may potentially change the outcome of the model, in more detail in the discussion.

Response: Unfortunately, we lack data with different benefit function. But we can still discuss this point.

First of all the shape of the benefit function describe the strength of selection on the interaction trait. For instance, we assume that the fecundity of host increases convexly with respect to the symbiont interaction trait, which models a strong selection on this trait. Thus reducing either the amount of optimal reward or the shape will modify the selection on this trait. And we expect that reducing the reward will made the transition more unlikely to occur. Moreover, reducing the reward will increase the cost of mutualism, which we know will reduce the transition probability. So, we need a reward sufficiently high so that mutualistic symbionts survive. This point has been highlighted in some paragraph:

line 263 page 6 in the Results:

"However, the transition can occur even in the absence of host competition, if the cost of mutualism is sufficiently low (e.g., a maximum cost of only 10% instead of 30% as in other simulations, details not shown). "

line 561 page 15 in the Discussion:

"Dependency may become absolute for a sufficiently high cost of mutualism, but in these conditions the transition to mutualism will not occur"

Moreover, at the beginning of the transition host is not mutualistic, so no reward. And the reward for the plant is large only if the plant is at low density globally. Otherwise, the global competition keep the reward small. Thus the reward is not the only process leading to the transition. We have shown that the transition indirectly results from the host competition that reduce parasitic symbiont viability. This point is explained in the Discussion:

line 340 page 10:

"Therefore, contrary to hypothesis H3, the transition is not directly caused by the higher fecundity of mutualistic pairs [which would fit soft selection, Wallace, 1975] but only indirectly by the increase in host competition, which renders areas dominated by parasites unviable (hard selection). However, this only occurs when competition between hosts is partly global (Figure 5b); if it is purely local, mutualistic clusters cannot influence the viability of parasitic regions and will suffer from kin competition. In line with hypothesis H4, local competition between hosts for resources thereby prevents the transition to mutualism. Local competition between hosts for available space also occurs when hosts disperse locally, but this does not jeopardize the transition."

4.5 Abstract

Abstract: "Spatial structure might be the key to this transition". This idea of spatial structure driving the transition is the core concept of the manuscript. It would be helpful to include in one sentence in the abstract the main argument why spatial structure may be so important.

Response: We have changed several parts of the abstract. The section concerning spatial structure now reads:

line 10 page 1:

"We hypothesize that spatial structure can lead to the formation of higher selection levels favouring mutualism. This resembles the evolution of altruism, with the additional requirement that the offspring of mutualistic hosts and symbionts must co-occur often enough."

4.6 Mutual dependence

Introduction: "For instance, aphids and their intracellular bacterial symbiont Buchnera aphidicola are irreversibly mutually dependent since the symbiont provides essential amino acids to its host [Akman Gündüz and Douglas, 2009, Bennett and Moran, 2015]". This sentence only states why the host is dependent on the symbiont, not the other way around. Since one talks about irreversible mutual dependence, it would be important to state also the other direction of the dependence.

Response: Roughly speaking, symbionts almost always depend on their host, whereas the reverse is not true. We have changed the corresponding section, which now reads :

line 108 page 3:

"Most symbionts cannot live freely and therefore completely depend on their host, but most hosts can complete their life cycle without their symbiont (e.g., in plant-ant, plant-fungi or legume-rhizobium mutualisms) and several reverse pathways are possible from mutualism to parasitism [Sachs and Simms, 2006, Werner et al., 2018, Week and Nuismer, 2021]. However in some cases hosts depend on their symbiont, for instance the intracellular bacterial symbiont *Buchnera aphidicola* provides essential amino acids to its aphid host [Akman Gündüz and Douglas, 2009, Bennett and Moran, 2015].

4.7 Probability of transition

Results: "Without dispersal cost, the transition is more likely to occur under strong competition than weak competition (see the probability of transition in Figure 2a))." I'd personally suggest including these probabilities also in the main text. Otherwise, if the reader needs to scroll down to look up the probabilities in the figure, it disturbs the flow of reading.

Response: We have removed these probabilities following comment 3.18 and replaced the boxplots by histograms. So we directly see from the histogram that without dispersal cost, the number of transition with weak competition is lower than the number of transition with strong competition. We have changed the caption of Fig.2:

Caption Figure 2

"Without dispersal cost there are a total of 86 transitions when the competition is weak and 951 when the competition is strong. With dispersal cost there are 1000 transitions whether the competition is weak or strong."

4.8 Density units

Results: Figure 2 panels B and C. What is the unit of host and symbiont density? Is this the proportion of cells filled with each species in the grid, or (for the symbiont) the proportion of hosts carrying a symbiont? It would be informative for the reader to include either in the axis label or in the figure caption a more descriptive explanation of what exactly the axes represent in the model.

The densities corresponds to the proportion of occupied cells. We add this information in the caption of Figure 2.

4.9 Definition of dispersal

Appendix A.1: Related to the mathematical implementation of dispersal in the model. For local dispersal, when n individuals would disperse, did you draw n times from a uniform distribution, so that potentially all n individuals could end up dispersing to the same of the 8 surrounding patches, or is there a form of kin avoidance, where all n individuals would move to a different patch (I assume the former). For global dispersal, is the target of dispersal chosen from a uniform distribution that includes the parental patch and local patches (i.e., can global dispersal end up being local), or are these 9 patches included the potential target patches? Perhaps it could be useful to include some more details (or equations) on the dispersal behaviour in the appendix, in case people are trying to understand or even recreate the model conditions.

To clarify this point we add the following paragraph in the Appendix A.1 and the Figure A5:

line 655 page 19:

"**Dispersal.** At each time step, hosts and symbionts produce offspring which can disperse over the landscape either locally or globally. For each agent, the proportion of its offspring dispersing globally is given by the dispersal trait ε. The location of offspring dispersed locally is chosen randomly uniformly over the 8 neighbors of its parents, while the location of those dispersed globally is chosen uniformly over the entire landscape expected the location of the parent (Figure A5 for the description of the local and global scale). In particular, a globally dispersed individual can arrive in the local neighbor of parents as the locally dispersed one. Moreover, the offspring are dispersed independently from each other and their location is chosen independently of the current landscape. In particular, offspring can arrive at an already occupied location and symbionts' offspring are not only dispersed in location where there is already an host. For instance if a host disperse $2/3$ of its offspring at large distance from it, its dispersal trait satisfies $\varepsilon = 2/3$. Then the $2/3$ of its offspring are dispersed randomly uniformly in the entire landscape (red stars in Figure A5) while the remaining $1/3$ is dispersed locally around it (red circles in Figure A5)."

4.10 Two dispersal modes

Related to this last comment, dispersal was implemented in the model using two very distinct mechanisms, global versus local dispersal, rather than for example working with a dispersal kernel. I can see why such a choice was made, both because it is also a realistic biological model (for example in plants, where heavy fruits may fall locally to the plant, but also be displaced far by a frugivorous species), and because it allows for a more clear distinction between the two strategies than when working with a dispersal kernel. Perhaps it may be useful to however provide some biological example in the supplement (similarly as for competition, where the difference between local and global competition is presented through a very nice example)?

We agree with the reviewer. We could have used a dispersal kernel with a parameter, describing the mean distance dispersal, which we define by the dispersal trait ε. For instance, let pick the Gaussian kernel K in one dimensions with zero mean and variance equal to 1. Then for an agent of dispersal trait ε in location x we may have taken the following dispersal kernel

$$K_\varepsilon(y) = \frac{\frac{1}{1+(\sqrt{2}L-1)\varepsilon} K\left(\frac{\|x-y\|}{1+(\sqrt{2}L-1)\varepsilon}\right) \mathbf{1}_\Omega(y)}{\int_\Omega \frac{1}{1+(\sqrt{2}L-1)\varepsilon} K\left(\frac{\|x-y\|}{1+(\sqrt{2}L-1)\varepsilon}\right) dy}$$

where Ω is the square lattice of size $L \times L$, with $L > 1$ and the size of cell is 1.

However, our approach allows us to clearly distinguish between local dispersal (short mean dispersal distance) and global dispersal (larger mean dispersal distance). Let us assume that the mean distance dispersal of hosts is the local neighbor but they can do long distance dispersal, that is they can disperse offspring far away from this local neighbor. However, their long distance dispersal ability may vary between hosts. For instance if an host disperse 66% of its offspring at long distance and 33% at short distance we end with the following case (see Fig.A3 in Appendix). Thus to clarify this point we add the paragraph "Dispersal" in Appendix, see previous comment.

Furthermore, in order to provide a biological example as suggested, we added the following in the model description:

line 182 page 4:

"These two modes of dispersal correspond to a mixture of short and long distance dispersal events. For instance, fleshy fruits may be dispersed either by small birds having a short-distance behaviour, or by mammals and large birds which disperse the seeds at long distances [Jordano et al., 2007]. Fruits may also remain unconsumed and fall locally. Depending on the fruit's traits, its propensity to be consumed by either type of frugivores may vary among individuals, which is captured by the dispersal trait ε."

5 Reviewer 5

5.1 General comments

Here the authors investigate an evolutionary path from parasitism to mutualism using a host-symbiont simulation model. While previous work has investigated the transition to mutualism in systems where symbionts are vertically transmitted, the present work studies this transition when symbionts disperse freely. Analysis of simulated results demonstrates that, alongside spatial structure emerging via the evolution of local dispersal, host competition plays a key role on this evolutionary path to mutualism. Overall, this is an interesting study that provides novel insight into the transition from parasitism to mutualism. The approach taken to simulation and analysis is, for the most part, nicely done. However, there are a few technical details that I found concerning and aspects of the writing that I think can be improved (see below). Assuming these issues and the writing will be ironed out, a revision of this preprint will make a nice contribution to the field. I found the introduction section to be well-written, providing both a solid motivation for this study and a satisfying review of previous work on the subject. However, the quality of writing deteriorated towards the end of the introduction and throughout the rest of the manuscript.

5.2 Local competition

In particular, when listing the goals of the study, the authors left out the question on the effect of local competition. In the results section, the effect of local competition on the transition to mutualism, while interesting, seemingly appeared out of nowhere. The description of competition earlier in the main text made no mention of local competition and there was no mention of investigating this phenomena in the introduction.

Response: We have included in the introduction:

line 101 page 2:

"Also, densely populated mutualistic clusters might suffer from intraspecific competition between hosts, unless competition acts on a large spatial scale."

line 130 page 3, in the list of hypothesis:

"**H4:** If competition between hosts in mostly local, this hampers the formation of mutualistic clusters, thereby preventing the transition."

5.3 Appendix and notations

The sections on model description, results and appendix A1 lacked consistent notation (see below). Some details in the appendix, such as the model of mixed local and global competition, should be moved to the main text for clarity.

Thank you for this remark (see comment 1.17 as well). We tried to fix this issue by adding some mathematical information in the Methods and providing more details in the Appendix. We also checked the mathematical notations.

5.4 Caption Fig.5

There are smaller aspects of the paper that made it difficult to follow. For example, in the caption of Figure 5 panels a), b) and c) are described in order, but then more information on panels a) and b) followed. It seems like it would be easier to read this caption if the information on panels a) and b) were kept together, especially since panel c) is presenting a relatively different result.

Response: We reformulated the caption of Fig.5 as follows:

"Figure 5: The role of host competition in the transition to mutualism. Effects of competition strength γ_c (panel a) and spatial scale w_h (panel b) on the percentage of mutualistic symbionts with dispersal cost $d = 0.45$ and after 10^4 time steps and over 50 replicates. Black curves is the median and shaded regions are 95% confident intervals. Dashed red line is the transition threshold of 10%. In panel a) competition is global ($w_h = 1$) and in panel b) competition is strong $\gamma_C = 0.2$. Panel c) represents the effect of competition on the transition and on the maintenance of mutualism (simulation without dispersal cost $d = 0$). Panel d) presents the effect of a reduction in competition caused by a perturbation eradicating all individuals in a large square. The perturbation occurs around $t = 10^4$, which is 5000 time steps after the transition. Other parameters are $m = 0.06$, $c_m = 0.3$, $f^h_{min} = 0.1$, $f^s_{min} = 2.5$, $f_{max} = 8$, $f^a = 0.5$ and $\beta_{max} = 0.5$"

5.5 Parasitic system viability

Viability of parasitic system: My greatest technical concern is the value chosen for the maximum expected offspring number of solitary hosts (which appears in the three notations fsh max, famax and fmax a throughout the main text and appendix). It seems like setting fsh max = 0.5 is problematic for this study since the host population (and therefore the whole system) would be doomed to extinction. A population where individuals have at most 0.5 offspring on average is not viable. Under these conditions there is no so-called parasitic system. Hence, it seems that the conditions for mutualism to evolve coincide with persistence of the system whenever $fshmax < 1$. I would be curious to understand how the results change when the solitary host population is (more) viable. In particular, what is the threshold maximum expected offspring number for solitary hosts 1 at which mutualism does not evolve? At least a ballpark estimate would be interesting (e.g., greater than one). Alternatively, demonstrating that mutualism usually does not evolve when maximum expected offspring number of solitary hosts is fixed to 0.5, but some other important parameter has been modified, would be sufficient to demonstrate that simulations are not rigged to force mutualism to evolve.

I think there is a miss understanding in the model description. The fecundity is per time step and not per generation. Our model consider overlapping generations. Thus, hosts alone will persist if $f^a > m/(1-m)$, where f^a is the fecundity of alone host per unit of time defined by equation (5), appendix A.1, and $0 < m < 1$ is the mortality rate. Thus, we choose fecundity and mutualistic cost parameters so that the persitence condition holds true. More precisely, with our parameters we have $m/(1-m) = 0.063$ and the minimal fecundity of host alone is $(1-c_m)f^a = 0.35$ (see appendix A.2 "an approximation of the parasitic system section for more mathematical details). As a result, the host system alone or the parasitic system is viable.

To clarify this point we add some mathematical analysis in appendix A.2

line 696 page 22:

"**An approximation of the parasitic system.** First, we aim to describe the expected proportion of sites occupied by hosts and parasitic symbionts at equilibrium. We assume no mutations of interaction or dispersal traits and hosts and symbionts disperse globally randomly over the landscape composed of N sites. According to our model, the dynamics of the proportion of sites occupied by the host alone ρ_{ha} or host with symbionts ρ_{hs} is given by

$$\begin{aligned}\rho_{ha}(t+1) &= (1-m)\rho_{ha}(t)\Big[\big(1-f^s(\alpha_h,\alpha_s)\rho_{hs}(t)\big)+f^{ha}(\alpha_h)\Big(1-\rho_h(t)^{\gamma_C}\Big)\Big]\\ &\quad +(1-m)\rho_{hs}(t)f^h(\alpha_h,\alpha_s)\big(1-\rho_h(t)^{\gamma_C}\big)\\ \rho_{hs}(t+1) &= (1-m)\rho_{hs}(t)\Big(1+f^s(\alpha_h,\alpha_s)\rho_{ha}(t)\Big)\end{aligned} \tag{16}$$

where $\rho_h = \rho_{ha} + \rho_{hs}$ is the total proportion of hosts and α_h and α_s are interactions trait of host and symbionts respectively. In this model, the traits are fixed – if $\alpha_s < \alpha_s^*$ symbionts are parasitic while there are mutualistic if $\alpha_s \geq \alpha_s^*$. Since the symbionts need host to survive, the proportion of sites occupied by symbionts is ρ_{hs}. Even if hosts and symbiont does not share the same mortality rate m, the model holds true by multiplying the terms f^s by $(1-m_s)$ the survival rate of symbionts instead of $(1-m)$. We can check that the following qualitative properties holds true with a different mortality rate. However, it will modify the quantitative outcome of the model.

For any given pair of interaction traits, we can compute the equilibria of this dynamical system.

Extinction. The extinction equilibrium, which corresponds to $\rho_{ha} = \rho_{hs} = 0$, always exists but it is unstable if

$$\frac{1}{f^{ha}(\alpha_h)}\frac{m}{(1-m)} = \frac{1}{(1-c_m\alpha_h)f^a}\frac{m}{(1-m)} < 1$$

We have picked parameters, which fulfill this criterion (Table 1). In particular, we can see from this formula that increasing the mutualism cost c_m can lead to non viability of more mutualistic host. In our simulations, we fix this value to $c_m = 0.3$."

5.6 Reproducibility

Another issue is with reproducibility. Although the description of the simulation seems to be thorough enough to reproduce this study, reproducibility can be improved by hosting the code for the simulation and subsequent analysis on a public repository such as github. This would also aid the reviewing process by allowing the reviewers to check the code directly.

Response: This was also suggested by comment 1.13. All codes are now available on a public github repository:
https://github.com/leoledru/PCI-Ledru-et-al.-2021-

5.7 Line numbers

The addition of line-numbers would aid the review process.

Response: Done

5.8 Recombination

In the case of sexual reproduction, recombination may relax the correlation between dispersal and interaction traits. Does this imply that sexual reproduction would inhibit the transition to mutualism under this model? Might be worth including in the discussion.

Response: Sexual reproduction would probably not inhibit the transition, only lengthen the waiting time. We added in the discussion the following:

line 457 page 13:

"**Asexual reproduction.** Many models of (co)evolutionary dynamics assume asexual reproduction [e.g. Kéfi et al., 2008, Loeuille and Loreau, 2005], especially within the framework of Adaptive Dynamics [e.g. Dieckmann et al., 1995, Loeuille and Loreau, 2005]. In the case of sexual reproduction, recombination may soften the correlation between dispersal and interaction traits, which is nevertheless essential to the transition. However, the work of Dieckmann and Doebeli [1999] on the coevolution between a niche and a mating trait showed that linkage disequilibrium can itself evolve, thereby preserving the correlation between traits. In the present case, we speculate that sexual reproduction would lengthen the waiting time until a successful transition, without hindering the transition in the long term."

5.9 Competition and dispersal

Since the evolution of local dispersal in many systems can lead to the evolution of local competition, I am curious how the results of this study change when competition occurs on the same scale as dispersal and therefore evolves in response to dispersal ability. This differs from the model of local/global competition described in the appendix since there the scale of competition is a fixed parameter. In particular, could a system that begins with global competition/dispersal transition to mutualism via the evolution of local competition/dispersal or does the evolution of local competition prevent this transition? Also might be worth discussing this in the main text.

Response: We have now specified in the methods that hosts compete via two distinct mechanisms, for space and for resources:

line 190 page 5:

"Hosts compete for empty cells, especially if they disperse locally. Beside space, hosts may also compete for resources."

Next, in the discussion we explained that only competition for resources prevents the transition:

line 345 page 11:

" In line with hypothesis H4, local competition between hosts for resources thereby prevents the transition to mutualism. Local competition between hosts for available space also occurs when hosts disperse locally, but this does not jeopardize the transition."

5.10 Typo

On page two, beginning of third paragraph: "With respect to altruism" should be "With respect to mutualism"?

Response: Done

5.11 Strong mutualism

Second paragraph under the subsection titled Fecundity rate and mutualism/parasitism: Is "strong mutualism" something that has been defined elsewhere? If so, please cite that source.

Response: "Strong mutualism" was defined following Wilson [1979], who defined "strong altruism" when altruism is costly (this is sometimes called "true altruism" as well), as opposed to "weak altruism" when altruism is more beneficial to members of the trait-group than to the altruistic organism. However, this terminological complication was unnecessary, so we chose to remove the corresponding sentences

5.12 Typo

Third paragraph under the subsection titled Fecundity rate and mutualism/parasitism: "We note interaction traits of the host and symbiont. . . " should be "We denote interaction traits of the host and symbiont by. . . ".

Response: Done

5.13 Mutation process

The section on mutation in the model description: What rates did you use in the exponential distribution for each trait and for each species? How are mutations accumulated? Is the exponential variable capturing a mutation simply added to the parental trait value? If so then mutations can only increase trait values, which is obviously problematic. Are the mutations actually added or subtracted depending on fair Bernoulli trials? This would be better since trait values can then decrease as well and mutation would not add bias to the evolutionary trajectories of each trait. If this is so, then the mutation model is better described by a mean-zero Laplace distribution than exponential. See https://en.wikipedia.org/wiki/Laplace-distribution

Response: Thank you for this remark. We were not really clear about the mutation process. We do clarify that mutation occur during reproduction and the trait of the offspring is chosen randomly around the parent trait.

We clarify this point in the Mutation paragraph of Methods section and in remark 1.3 and 2.7.

5.14 Notation redundancy

Section on dispersal: The cost of global dispersal d has already been used as a parameter limiting the size of mutations. Please pick a different symbol to clarify notation.

Response: We changed the notation for the mutations.

5.15 Local and global competition

Section on competition: Since one of the results was the effect of local competition on the transition to mutualism, it would be best to include information on both models of competition (the purely global model and the mixture of global and local model) in the main text. Otherwise, the result on the effect of local competition

Response: To explain more in detail the different types of competition, we move some equations and explanations from the appendix to the Methods section.

line 190 page 5:

"Hosts compete for empty cells, especially if they disperse locally. Beside space, hosts may also compete with each other for resources like water, light or food. In order to test hypothesis H3 we introduced intraspecific density-dependent competition, acting either at the local or the global scale. For instance, competition for light only involves the closest neighbors while competition for the water table might act at the entire space scale. The competition scale parameter w_h, ranging in $[0, 1]$, weights the effect of the local density ρ_h^{local} and the global density ρ_h^{global} of host on the competition. Competition reduces the establishment probability P_I of the offspring:

$$P_I = 1 - \left((1 - w_h)\rho_h^{local} + w_h\rho_h^{global}\right)^{\gamma_C} \tag{17}$$

The local host density ρ_h^{local} corresponds to the host density in the 8 neighbouring cells surrounding the offspring, while the global density ρ_h^{global} corresponds to the host density over the entire landscape (see Figure A2 for a schematic representation). The parameter γ_C corresponds to the competition strength. The competition is strong when $\gamma_C < 1$ (sub-linear function), while it is weak when $\gamma_C \geq 1$ (super-linear function)."

5.16 Coevolution

Beginning of fourth paragraph in results section: What is coevolving with dispersal? I believe you mean the interaction trait in coevolves with the dispersal trait in both species during the transition to mutualism.

Response: We remove this sentence in the new version of our manuscript.

5.17 Introducing local competition

Subsection titled Effect of competition: The authors report results on the effect of local competition. This is interesting, but caught me off guard as the model of local competition had not been introduced or mentioned in the model description. From the outline of the competition model in the model description section, I understood that competition was always global. Looking in the appendix, I see there is a description of local competition. It would be best to mention this in the main text.

Response: Please refer to our response to comment 5.2

5.18 Unclear sentence

Subsection titled The role of quasi-vertical transmission: The statement on mutualistic phenotypes retaining their global dispersal ability is confusing. Something like, "a significant fraction of individuals with mutualistic phenotypes also dispersed globally, in contrast to the tendency for local dispersal and mutualism to coevolve" might communicate this point with more clarity.

Response: We have changed this sentence accordingly:

line 399 page 12:

"... a significant fraction of hosts with mutualistic phenotypes also dispersed globally ($\sim$ 40%, Figure 3), which partly counteracts the necessity of quasi-vertical transmission."

5.19 Irreversibility

Subsection titled Host dependency and irreversibility of the transition: I understand that the transition to mutualism is reversible if the competition among hosts declines. Is this also true if competition among hosts becomes local?

Response: We added in the discussion that:

line 576 page 15:

"Although this has not been tested formally, the reversion is also very likely to occur if host competition for resources shifts from global to local, since it is apparent from Figure 5b that local competition completely prevents mutualism, even in the presence of dispersal cost."

5.20 Fecundity rate

The term fecundity rate makes it sound like a continuous time model where offspring are produced at a specific rate. This confused me since the authors develop a discrete-time model. I think replacing the term fecundity rate with something like offspring number would be less confusing.

Response: We agree with the reviewer that fecundity rate is not appropriate. Thus, we define fecundity in our paper as the average offspring number of an agent because our parameter f ranges in $[0, 8]$ and it is not necessary an integer. Indeed, the number of offspring at each time step is sample from a Poisson distribution with parameter f. We add the following sentence in our manuscript:

line 162 page 4:

"Each agent produces offspring according to a Poisson distribution with parameter f, which corresponds to its fecundity. The fecundity defines the average number of offspring per agent. "

5.21 Interpretation of a parameter

What is the significance of γ_f ? Why is it interesting to include in the model? Why is it only applied to host and not symbiont?

Response: The parameter γ_f represents the strength of selection on the interaction trait α_s through the interaction between a host and a symbiont. Indeed, if γ_f is large then the fecundity is picked around the mutualistic trait $\alpha_s \sim 1$ of symbionts, so they should be selected from the host point of view. In our study, we take $\gamma_f = 4$ corresponding to a strong selection. A similar parameter is present for the symbiont fecundity. However, we states this parameter to 1. Thus, we put a weaker selection pressure on the hosts interaction trait α_h than on the symbiont interaction trait α_s.

Moreover, the effect of the two parameters are different. For hosts, the associated symbiont can be either parasitic or mutualistic depending on its trait α_s, as explained in section "Mutualism/parasitism

threshold" in appendix A.1. We choose the parameter γ_f such that the symbiont trait threshold α_s^* between a parasitic and a mutalistic symbiont is around 1/2. We pick this value such that the trait range for parasitic and mutualistic symbionts have the same size. For symbionts, hosts are always beneficial because they are obligate symbionts. We model this interaction with a minimal fecundity of symbiont in interaction with host equal to $f^s_{I,min} \gg 1$.

We clarify this point in the method by adding

line 166 page 4:
"γ_f describes the selection strength on the trait α_s – the selection strength on α_h is set to $\gamma_s = 1$."

and *line 625 page 16* in the appendix A.1:
"The coefficient γ_f corresponds to the selection strength on the interaction trait α_s. Using a coefficient $\gamma_f > 1$, we create a convex function allowing a transition from parasitism to mutualism for a central value of the symbiont interaction trait. However, note that modifying the shape of this fecundity curve (from concave to convex via linear) does not qualitatively change our results."

5.22 Typo

There appears to be a typo in equations (2). In particular, setting $\alpha_i = 1$ for either i = h or i = s does not return fI, max. Instead, if the authors dropped the second fiI, min appearing between cif and α_i, these equations would return fI, max. It's unclear whether this was a typo and if so whether the simulations inherited it.

Response: Thank you for this comment, we actually make a typo in the formula corrected now. In the code of the simulation we actually take the following form:

$$f^h_I(\alpha_s) = f^h_{I,min} + \big(f_{I,max} - f^h_{I,min}\big)\alpha_s^{\gamma_f}$$

$$f^s_I(\alpha_h) = f^s_{I,min} + \big(f_{I,max} - f^s_{I,min}\big)\alpha_h$$

5.23 Figure A1

From this figure it appears that symbionts do not disperse. However, it seems like they should disperse freely since they are not vertically transmitted.

Response: Thank for your remark, we forget to put dispersal on the arrow before establishment (see new Fig.A1). So the offspring symbionts do disperse by themselves after they are produced. This dispersal is totally independent from the host dispersal. However, the establishment success does truly depend on the presence of a host at the dispersed location.

5.24 Caption for Figure A1

Instead of calling it a numerical algorithm, please refer to it as a simulation or, even better, an individual-based or agent-based simulation. Although it technically is a numerical algorithm, simulation is the more colloquial phrase.

Response: Thank you for this remark, we changed the word numerical algorithm in caption of Figure 1 by
"Figure 1: Sketch representation of the individual based model."

5.25 Useless sentence

Sentence following Figure A1: This sentence is redundant and confusing. I think the point would be clarified without it.

We removed the sentence.

5.26 Cost of mutualism

Why should the host be affected by its mutualism cost when it is not engaged in the interaction? In the following paragraph the authors claim that the cost is a developmental cost. However, I'm not sure what this means. I would like to know some biological examples that motivate this reasoning. The motivation

for the competition component of the model beneath Figure A2 is a good example of what I would hope to see for the developmental cost component of the model.

Response: In the methods, we removed the unclear statement about development. In the discussion, we added the following:

line 439 page 13:

"Moreover, in the model some cost is paid even if the partner is parasitic or if the host is free of symbiont. For instance, domatia or extrafloral nectaries are unconditionally produced [Bronstein, 1998], even though domatia size can be plastic [Kokolo et al., 2020]. Also, plants produce costly floral displays even in the absence of pollinators."

5.27 Eqn (7)

Just a small point on notation. The spatial scale parameter cs looks like it should be affiliated with the symbiont. Something like ψ_h may be less confusing.

Thank you for the comment, we changed the notation to w_h.

6 Other changes

During the revision, we came through other ideas that deserve some attention in the manuscript. We detail below the changes that have been done.

6.1 Intra-host dynamics

If the assumption of mono-infection is relaxed, two different strains of symbionts may colonize the same host and compete with each other. This possibility has been included in Appendix A.7 and discussed in the section "Symbiont competition within hosts" of the discussion.

line 465 page 13:

"**Symbiont competition within hosts** We previously assumed that only a single symbiont could infect a host, however several strains may compete within the same [Bongrand and Ruby, 2019, Zytynska and Weisser, 2016, Alizon et al., 2013]. The host may be able to prevent the proliferation of parasitic strains [Sachs et al., 2010b], but parasitic strain may also overcome the others, which could prevent the evolution of mutualism [Jones et al., 2012]. An extension of the model, presented in Appendix A.7, includes superinfections where mutualistic symbionts can be dislodged by parasites reaching the same host. When superfinfection probability rises above 50%, the transition is prevented, otherwise mutualistic symbionts can persist, although at lower densities than without superinfections (Figure A15). Thus, although superinfections are clearly detrimental to the transition, mechanisms favouring the evolution of mutualism in our present model can resist some degree of competitive exclusion by parasites."

line 793 page 27:

"**Symbionts competition within hosts** In our current model, a host can be colonised only by one symbiont and once the symbiont is established on a host, it cannot be replaced by another symbiont. Furthermore, when several symbionts arrive at the same time on an available host, the symbiont, which establishes, is chosen randomly uniformly among the contenders. Here, we relax these assumptions in order to model symbionts' competition within a host, or "superinfection". We assume that within a host, the most parasitic symbiont, with the lowest interaction trait, is the most competitive symbiont. Thus, it will be more efficient to establish in a host or dislodge a symbionts from the host.

Establishment of symbionts on a host. Specifically, when N symbionts, with trait $\{\alpha_1, \dots, \alpha_N\}$ arrive on a host, the establishment probability P_e^i of the symbiont i is given by :

$$P_e^i = \frac{p_i}{\sum_{i=1}^{N} p_i} \quad \text{with} \quad p_i = \min\left(\max\left(\frac{1}{N} - (\alpha_i - \bar{\alpha})\, S_{max}, 0\right), 1\right), \quad \text{and} \quad \bar{\alpha} = \frac{1}{N}\sum_{j=1}^{N} \alpha_j \tag{18}$$

where S_{max} measures the superinfections' intensity, which corresponds to the maximal competitive advantage of a symbiont. For instance, when a truly parasitic symbiont $\alpha_1 = 0$ tries to establish with a

truly mutualsistic symbiont $\alpha_2 = 1$, its establishment probability is $P_e^1 = (1 + S_{max})/2 \geq 1/2$. The establishment probability of the mutualsitic symbiont is $P_e^2 = (1 - S_{max})/2 \leq 1/2$. If $S_{max} = 0$, they have the same probability of establishment, while if $S_{max} = 1$, the parasitic symbiont always over-competes the mutualistic symbiont.

Replacement of a resident symbiont When N symbionts with trait $\{\alpha_1, \ldots, \alpha_N\}$ arrive in a host already occupied by a resident symbiont with trait α_s, they may dislodge the resident. Specifically, the probability of the resident symbiont to persist P_p is given by

$$P_p = \min\left(1 - (\alpha_s - \bar{\alpha})S_{max}, 1\right) \quad \text{with} \quad \bar{\alpha} = \frac{1}{N}\sum_{i=1}^{N} \alpha_i. \tag{19}$$

In particular, if the resident has a trait α_s lower than the mean trait of the invaders $\bar{\alpha}$, then the resident always persists. Otherwise, the resident may be dislodged with a probability smaller than S_{max}. Then if the resident is dislodged, the establishment probability of the N invader symbionts is given by the previous formula (18).

Figure A15 shows the effect of the superinfection intensity S_{max} on the percentage of mutualistic symbionts. We show that despite the competitive advantage of parasitic symbionts when competing for a host, the transition to mutualism is possible when the superinfection intensity is not too large (if $S_{max} < 1/2$, transition occurs, that is the percentage of mutualistic symbionts stays above 10%). Moreover, when $S_{max} < 1/2$, the trait distribution of symbionts is bimodal. ”

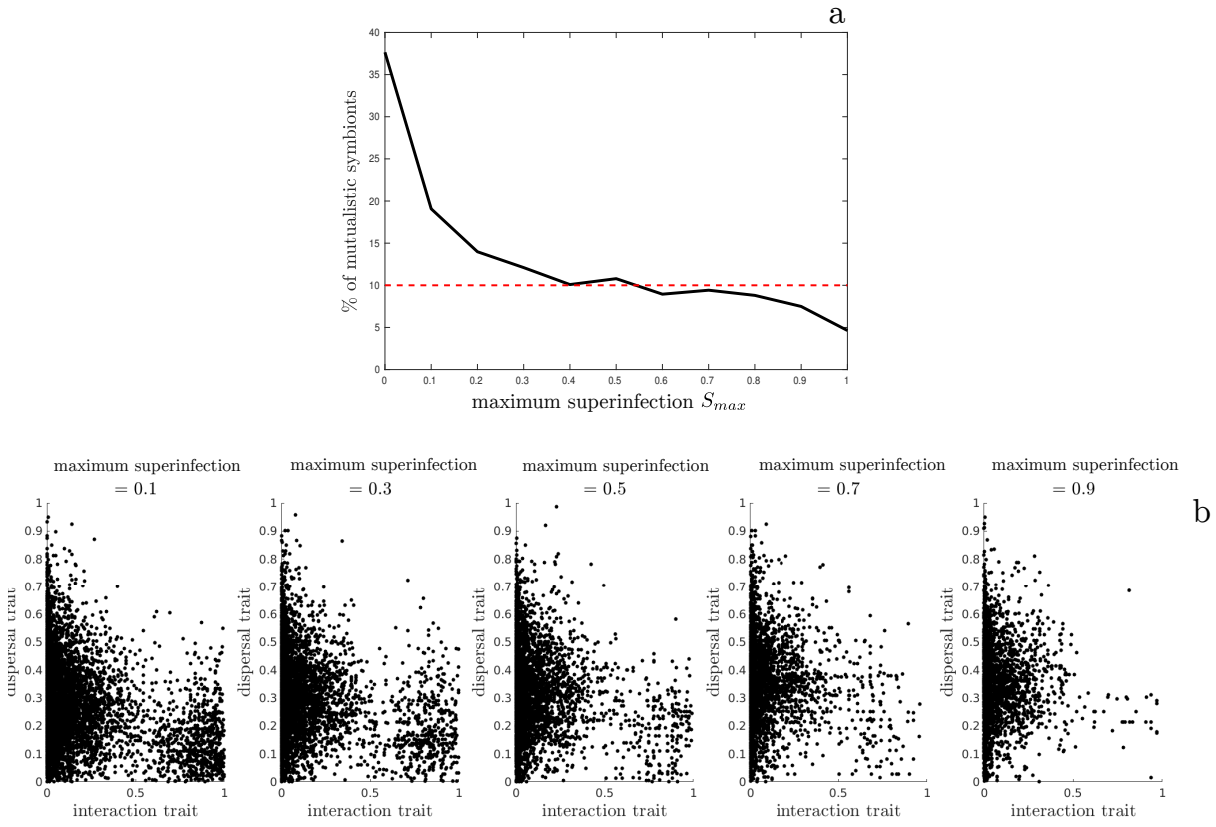


Figure 7: A15 – a) Percentage of mutualistic symbionts in function of the maximum superinfection advantage S_{max} averaged over 20 simulations per parameter values. b) Distributions of symbionts population in traits domain according to five intensity of superinfection advantage S_{max}. Distributions corresponds to 20 simulations for each parameter values. These results are obtained with a maximum time projection of 5000 time steps, a strong and global competition ($\gamma_C = 0.2$) and a dispersal cost ($d = 0$). Others parameters are $m = 0.06$, $c_m = 0.3$, $f^h_{min} = 0.1$, $f^s_{min} = 2.5$, $f_{max} = 8$, $f^a = 0.5$ and $\beta_{max} = 0.5$.

6.2 Aggregation index

In our study, we have investigated the spatial autocorrelation among hosts and symbiont and between host and symbiont. We have shown that neighbouring organisms have similar interaction traits. However, the assortment index does not inform us on the spatial aggregation of the hosts or symbionts distribution. To go further, we investigated the spatial aggregation of hosts and mutualistic and parasitic symbionts using an aggregation index described in appendix A.2 "Aggregation index". We show that hosts are more aggregated than symbionts which is expected because symbionts need a host to live. More interestingly, we show that parasitic and mutualistic symbionts have the same spatial signature after the transition, which is surprising because parasitic symbionts disperse more globally than mutualistic symbionts; we expected more aggregation among mutualistic than parasitic symbionts. This is because parasitic symbiont invade the neighborhood of the mutualistic clusters where hosts produce more offspring, parasitic symbionts therefore become aggregated around the mutualistic clusters. We stress this point in the Results section,

line 254 page 6:
"The aggregation indices (appendix A.1) behave similarly, after the transition the spatial aggregation of hosts, parasitic symbionts and mutualistic symbionts all increase, and the parasitic and the mutualistic symbionts reach the same level of aggregation (Figure A7)."

and in the discussion, *line 319 page 9:*
"Parasitic symbionts become themselves aggregated (Figure A7 since they develop around the mutualistic clusters, at their expense (Figure 4 c)."

We detail the mathematical background of this point in appendix A.1 "Aggregation index".

line 684 page 21:
"**Aggregation index.** From the assortment index analysis, we show that the symbionts and hosts are spatially assorted according to their trait. Now we aim to investigate how they are aggregated in space. We use a relative aggregation index $\mathcal{A}$ based on a measure of the number of pair of neighbors. More precisely, we define for any spatial configuration the number of pairs of neighbors P where a neighbor of an individual is its 8 closest cells. For instance, Figure A2 provides a schematic representation of a host spatial configuration and the dashed square represents the neighborhood of the red individual. The number of pair of the red individual is 3 in this example. Then for any spatial configuration with n individuals, we can define the maximal number of possible pair of individual which is given by $P_{max} = 4n - \lceil 6\sqrt{n} \rceil$ [Harary and Harborth, 1976]. Thus, we define the aggregation index $\mathcal{A}$ as the ratio between P and P_{max}:

$$\mathcal{A} = \frac{P}{P_{max}}.$$

We compute the aggregation index over time for the hosts, the parasitic symbionts ($\alpha_s < \alpha_s^*$) and the mutualistic symbionts ($\alpha_s \geq \alpha_s^*$) (Figure A7).

Hosts are always more aggregated than symbionts. Moreover, after the transition occurred, mutualistic and parasitic symbionts have the same spatial signature in terms of aggregation. This pattern was already observed in Figure 4 where we see mutualistic clusters surrounded by parasitic clusters."

6.3 Cheating

We discussed to what extent our model also accounts for the evolution of cheating in mutualism (paragraph "The evolution of cheating" in the discussion).

line 475 page 13:
"**The evolution of cheating.** Our main interest was to understand how mutualism can evolve from a parasitic relationship [Roughgarden, 1975, Drew et al., 2021] but mutualism may also have evolved in the first place, the classic evolutionary problem in this case being how can it resist to the invasion of "cheaters" [e.g. Sachs et al., 2010a, Jones et al., 2015, Ferriere et al., 2002]. According to Jones et al. [2015], cheating "(1) increases the fitness of the actor above average fitness in the population and (2) decreases the fitness of the partner below average fitness in the partner population". The latter condition is always satisfied by parasitic symbionts, but the former remains to be checked. Simulations starting

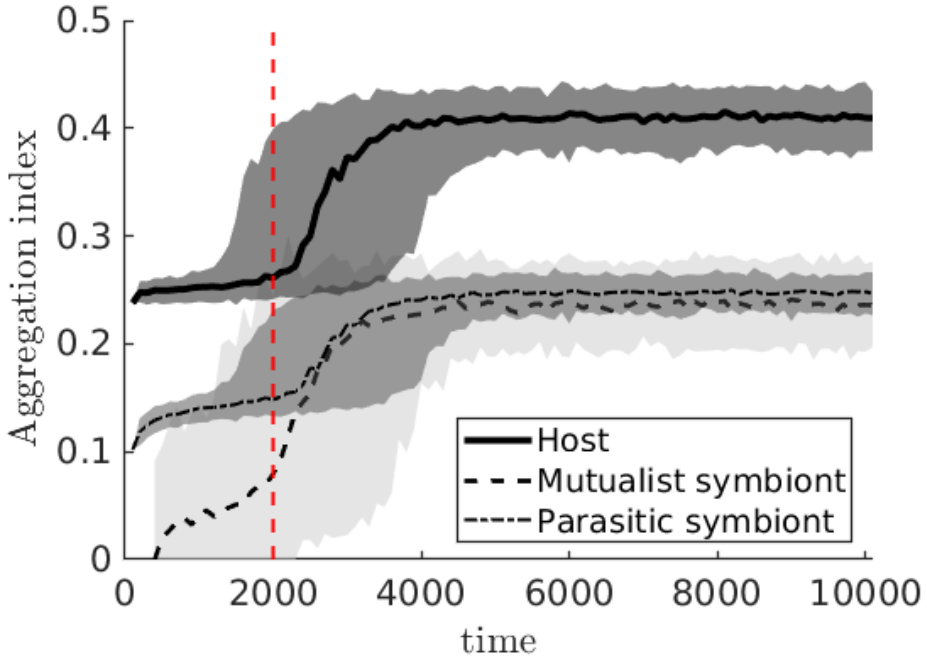


Figure 8: A7 – Aggregation index of the spatial distribution of hosts (plain curve), parasitic symbionts (dash-dotted curve) and mutualistic symbionts (dashed curve) over time. The shadow regions corresponds to the 95% confident interval and curves corresponds to the median over 100 replicates. The parameters are similar as Figure 4.

with mutualistic symbionts only are rapidly invaded by parasites, leading to an evolutionary equilibrium identical to the one reached by Figure 2c (details not shown). The population-level fitness [sensu Metz et al., 1992] of parasites is therefore positive when they are rare, thereby satisfying condition (1), and it gradually decreases to zero until the evolutionary equilibrium is reached. Hence, our model also accounts for the invasion by cheaters of an initially mutualistic system, leading to a coexistence of both strategies. Mutualism may also evolve from a competitive interaction, if two competitors start exchanging resources, each being a better exploiter of the resource it provides, and limited by the resource it receives [De Mazancourt and Schwartz, 2010]. However it is unknown to what extent this kind of mutualism is sensitive to cheating; spatial effects similar to those studied here might stabilize it."

6.4 Organisms

Given that 1) the concept of biological individuality can apply to other levels of organisation than organisms, and 2) the issue of evolutionary individuality appears in the discussion, we used the terms "organisms", "organismal", etc, when referring to hosts and symbionts, instead of "individuals".

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