

Project I — Computational Biology 2020-2021
Does high cost minimize the production of public good?

The potential for cooperators to establish themselves in a non-cooperative populations, or, conversely, for selfish individuals to invade and possibly destroy a cooperative population has mostly been formulated in terms of relative costs and benefits of the 2 populations. This is true both in the context of 'group selection' and in the context of 'kin selection' as well as the well known game theoretical models of cooperation (prisoners dilemma, hawk and dove). The general model result is that cooperation should not be too costly, or it will not persist.

Investigate these results in the context of a 'public good production'. Make sure the public good decays fast. Many micro-organisms secrete products in the medium to digest food sources and/or to enable the uptake of essential resources. Sidophores are a pre-eminent example. The production is generally costly, whereas the products and therewith benefits are shared by all in the environment.

Assume that both the cost of production and the benefits are proportional to the amount produced/used. First assume the cost of production of a unit of public good is low relative to its benefit. (e.g. a ratio 1:10) and study invasion of bacteria who produce more or less public good. and then study what increasing costs does to these invasion properties. After these ecological experiments, let production of public good evolve.

Compare your model and your results to the article by Ohtsuki *et. al*¹ Can you check if, under certain parameter settings there is quantitative agreement?

Discuss your finding in the light of at least one relevant, recent paper.

¹Ohtsuki, Hisashi, et al. "A simple rule for the evolution of cooperation on graphs and social networks" Nature 441.7092 (2006): 502-505.

Project II — Computational Biology 2020-2021
Why do animals/cells die?
Evolution of programmed death

Many organisms die because they are eaten or because of some accident. However even without such mishaps, they have a finite lifetime. The lifetime of closely related species can vary by an order of magnitude. Moreover it has been experimentally shown that simple (knockout) mutations can increase the lifespan (e.g. *Extended longevity in mice lacking the insulin receptor in adipose tissue* M Blüher, BB Kahn, CR Kahn - Science, 2003). In other words it is apparently possible to live longer, and we should therefore conclude that the extant lifetime of a species is an “evolutionary choice”. Explanations have been sought in terms of continued evolutionary adaptability to changing environments, or in terms of trade-offs (e.g. longer lifespan implies less fecundity) but data do not support this notion.

Here we will ask if and how higher death-rate could give a long term competitive advantage in a constant environment due to emergent pattern formation?

You can for example explore this problem in a system of predators and preys.

First study ecological dynamics between species differing in death rates, and look for example at the following

- Who out competes whom?
- Can otherwise identical lineages with different death rates coexist? Why?
- If you find coexistence, test whether the different evolved lineages without the other? (i.o.w., can high or low death rate lineages be 'rescued' by lineages with other death rates?)

Next, study how death rates evolve (focus on the interesting cases you found from the questions above).

Compare your results with results/discussions found in the literature, e.g. in similar models (discuss both differences in the model/experiments and in the general discussions).

Project III — Computational Biology 2020-2021
Influence of HGT on the information threshold

The Error Threshold describes the phenomenon that, given that replication isn't 100% accurate, survival of the fittest may not hold. As described in the lectures and in one of the practical questions, this error threshold depends on how much faster the "fittest" replicator replicates compared to its mutants. Survival of the fittest holds if:

$$\text{quality of replication} > \frac{a_2}{a_1} = \frac{1}{\sigma} \quad (1)$$

a_1 and a_2 are replication rates of master and mutants, respectively
 σ is the selection coefficient a_1/a_2

In the simple ODEs from the practicals we have studied this problem in well-mixed conditions with an infinite population size. We have also studied the problem in a CA with finite populations and stochastic dynamics. The latter problem is often described as Mullers Ratchet: the unavoidable accumulation of deleterious mutations.

In this mini-project, study the influence of horizontal gene transfer (HGT) on the Error Threshold. Focus on the following questions:

- Does HGT alleviate or hamper this Error Threshold? What are the conditions?
- How do these effects of HGT depend on possible risks of HGT?
- In a spatial model, study whether HGT can evolve and study which features of genes and HGT can help to strengthen your results
- Consider the work by Takeuchi *et al.*². How does your model compare to this study? What is similar/different?

Discuss your results in the light of other (more recent) literature.

²Horizontal gene transfer can rescue prokaryotes from Muller's ratchet: benefit of DNA from dead cells and population subdivision, Takeuchi et al., 2014

Project IV — Computational Biology 2020-2021
Speciation in space

Since the very start of evolutionary biology, scientists have wondered how new species come to be. What could cause one population of similar individuals to diversify into two or more distinct lineages? One such cause can be competition for resources. In the exercises, we saw that Dieckmann and Doebeli made a model in which competition for resources could make a population split, given that individuals were relatively specialist in their resource use³. The model cited was a well-mixed one. Many real-life populations however, are not well-mixed. So here, we will ask the question we have asked many times before: how will this system behave in space?

- Start with the model described by Dieckmann and Doebeli⁴, and implement a simple variant of this in a *CA*.
- Do you find speciation? If so, how do the conditions compare to those found in [3]?
- How are your results influenced by spatial pattern formation?
- *EXTRA*: Rather than making all individuals equally specialist, you could make specialism or generalism evolvable (think about tradeoffs!).

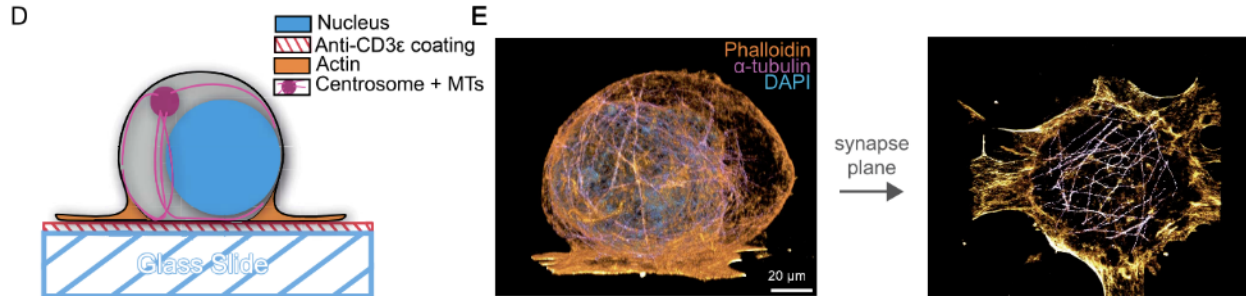
What do your results say about the likelihood of sympatric speciation? Compare what you found to results seen in the literature (both experimental and theoretical).

³U Dieckmann and M Doebeli - "On the origin of species by sympatric speciation" - Nature, 1999

⁴The model is described under the Methods section.

Actin reorganization upon T cell activation

Explaining complex biological reorganization through basic phenomenological rules.



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The ACT-CPM model tries to explain the behaviour of T lymphocyte (T cell) motility from the idea that the Actin villipodia and kinapse architecture give a measure of persistence to the leading edge of the moving cell ⁶. The T cell changes conformation once it finds an antigen presenting cell (APC). Recent experimental work has shown clearly how the actin network rearranges upon this activation, with an actin-depleted center and a dense ring forming ⁷. Can this process also be explained through persistence of actin?

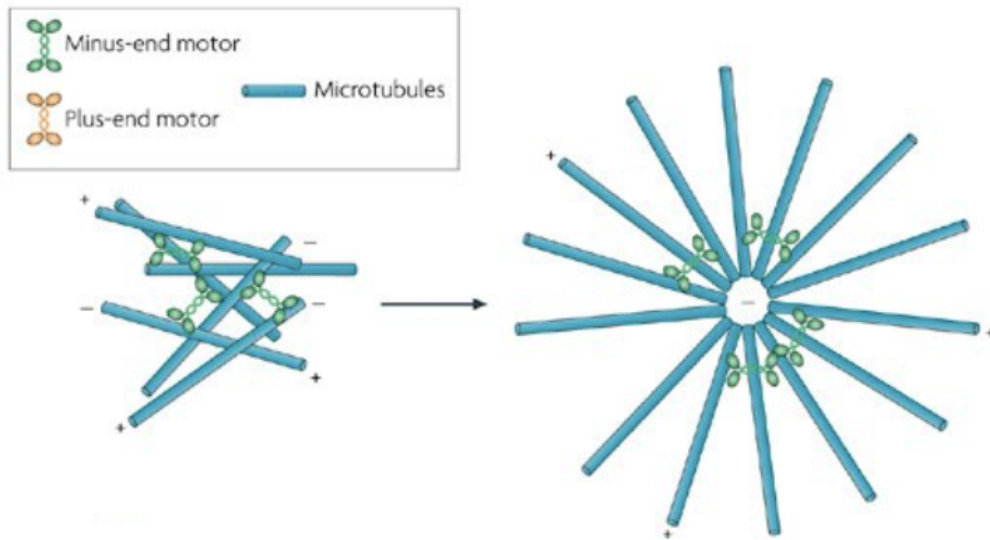
- Make the T lymphocyte model from Niculescu *et al.*[6], using the code hosted on <https://github.com/ingewortel/artistoo>. See also this action-packed example: <https://artistoo.net/examples/ActModelInteractive.html>.
- Devise a basic model for the APC (hint: the MHC-mediated response would induce a very tight cell-cell contact between the T cell and APC)
- Does this model recapitulate the findings of Murugesan *et al.*[7]? How do the parameters or model setup affect the behaviour of the reorganization?

⁵ Image from: Dynein self-organizes while translocating the centrosome in T cells, Gros OJ, Damstra HGJ, Kapitein LC, Akhmanova A, Berger F, 2020 (unpublished)

⁶Niculescu I, Textor J, de Boer RJ (2015) Crawling and Gliding: A Computational Model for Shape-Driven Cell Migration. PLOS Computational Biology 11(10): e1004280.<https://doi.org/10.1371/journal.pcbi.1004280>

⁷Murugesan S, Hong J, Yi J, Li D, Beach JR, Shao L, Meinhardt J, Madison G, Wu X, Betzig E, Hammer JA. Formin-generated actomyosin arcs propel T cell receptor microcluster movement at the immune synapse. J Cell Biol. 2016 Nov 7;215(3):383-399. doi: 10.1083/jcb.201603080. Epub 2016 Oct 31. PMID: 27799367; PMCID: PMC5100289.

Project VI — Computational Biology 2020-2021
Assembly of dynamic polar microtubule systems



⁸ Many cells rely on centered polar microtubule (MT) architectures to organize the transport within the cell, where a single point originates most/all of the MTs in a microtubule organizing center (MTOC). A classic example is the centrosome structure, which can also nucleate MTs. A disorganized network can easily be organized into such a polar MTOC (a centriole) by dynein motors (Cytrynbaum *et al.*, 2004)⁹. If a dynein motor walks on one MT and uses the other as cargo, they will pull the MTs together, if the dyneins hold onto the tips of the MTs, this causes all MT plus ends to gather in the same point. In this way a polar MT architecture is organized. The centrosome also enforces a polar structure, but does this from a predefined single point. How does the self-organizing system behavior compare to the centrosomal system¹⁰?

- Build a simulation in Cytosim, hosted on: <https://gitlab.com/f.nedelec/cytosim>, where you define MTs and dyneins that are able to use the MT as cargo. See https://gitlab.com/f.nedelec/cytosim/-/blob/master/doc/tutorials/tuto_self.md for help.
- Does this system self-organize into a polar structure? Why/why not?
- Is the system still stable if you add MT growth/shrinkage dynamics? Characterise the necessary components to stabilize the polar system.
- EXTRA: How does the confining shape influence this organization? Do you find non-circular polar systems?

⁸Image from: Karsenti, E. Self-organization in cell biology: a brief history. *Nat Rev Mol Cell Biol* 9, 255–262 (2008). <https://doi.org/10.1038/nrm2357>

⁹Cytrynbaum EN, Rodionov V, Mogilner A. Computational model of dynein-dependent self-organization of microtubule asters. *J Cell Sci.* 2004 Mar 15;117(Pt 8):1381-97. doi: 10.1242/jcs.00919. Epub 2004 Mar 2. PMID: 14996905.

¹⁰Letort G, Nedelec F, Blanchoin L, Théry M. Centrosome centering and decentering by microtubule network rearrangement. *Mol Biol Cell.* 2016;27(18):2833-2843. doi:10.1091/mbc.E16-06-0395