A somatic genetic clock for clonal organisms

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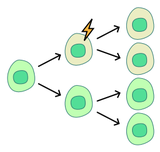
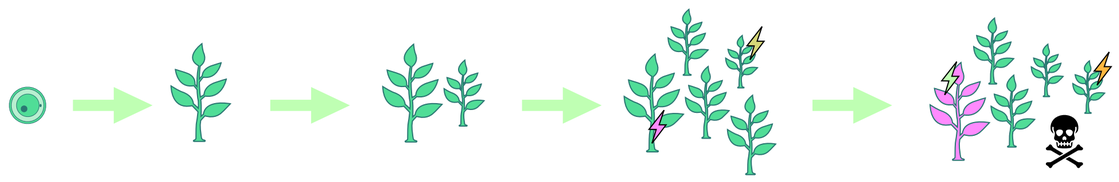
1. Somatic genetic clock

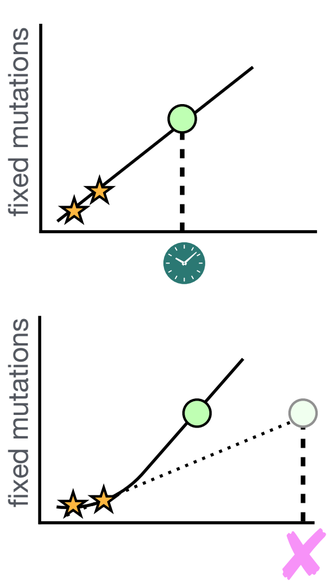


Cells accumulate somatic mutations when they divide, leading to somatic genetic variation within

Clonal organisms grow from a single zygote by repeating modules. Somatic mutations become fixed in modules by neutral drift [1].



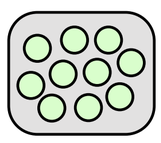
Fixed mutations accumulate linearly [2] and could provide a somatic genetic clock to estimate the age of clonal organisms.



Can calibrate the clock with clones of known age.

Problem: mutations do not fixate instantaneously, thus it takes time to reach linearity.

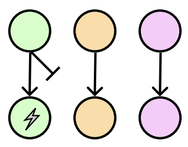
3. Model of a clonal organism



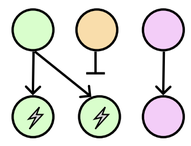
Clonal organism represented as a collection of *modules* that consist of *cells*. Modules grow to *N* cells by symmetric cell division at rate *b*.

At division cells obtain μ new mutations on average. Cells in homeostatic modules continue to proliferate by:

asymmetric division

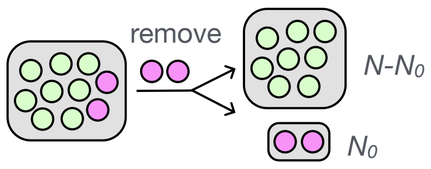


or **symmetric division.**

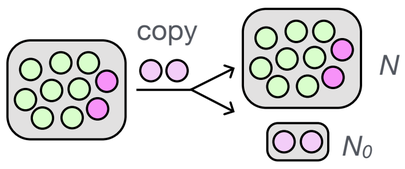


Homeostatic modules produce new modules at rate *r* by:

splitting



or **branching.**



3. Quantifying the delay to linearity

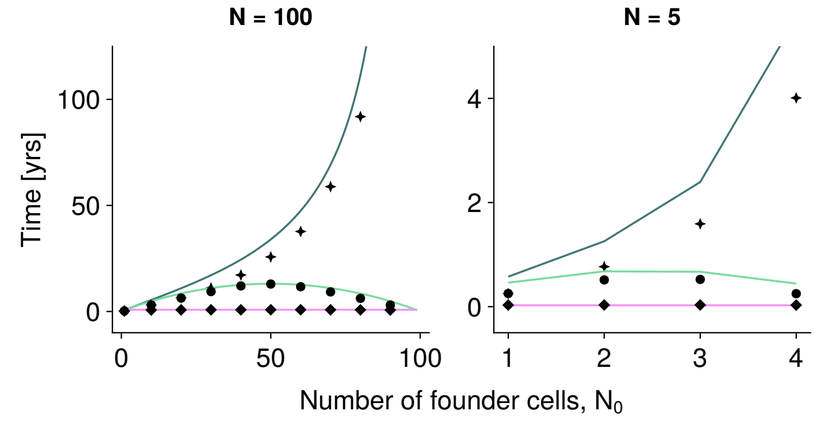
The time to reach linear accumulation is related to the conditional fixation times T.

Fixation by **symmetric cell division** in homeostatic modules is a Moran process: $T \approx b/N$ [3].

Repeated formation of new modules is approximated as a modified Wright-Fisher process:

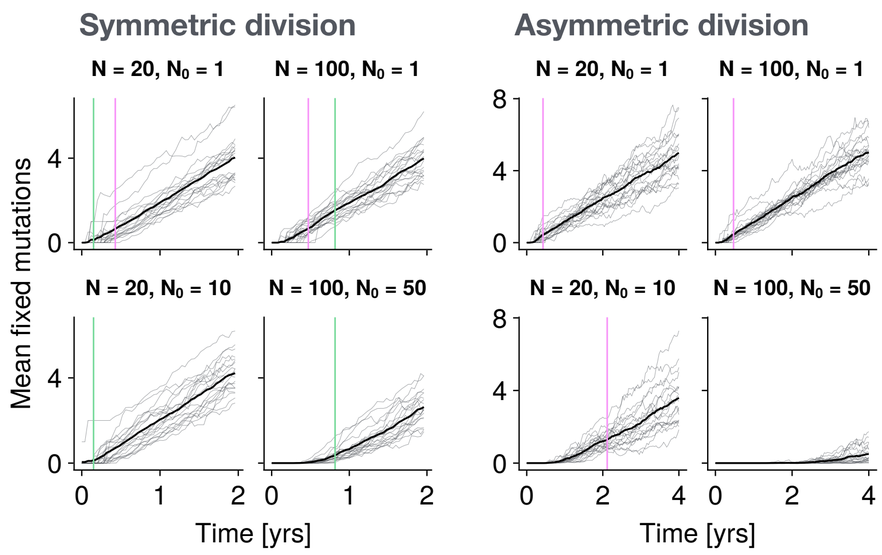
branching: $T \approx \frac{4N_0}{r\left(1-(N_0/N)^2\right)}$ **splitting:** $T \approx \frac{4N_0}{r}\left(1-N_0/N\right).$

Comparing theory and simulation:



✦ asymmetric division & **branching**
● asymmetric division & **splitting**
◆ **symmetric division** & **splitting**

Longer fixation times correspond to a longer delay to linearity:



4. Conclusions

The somatic genetic clock can be applied when linearity is reached quickly, e.g. for small modules, small initial modules or symmetric cell division.