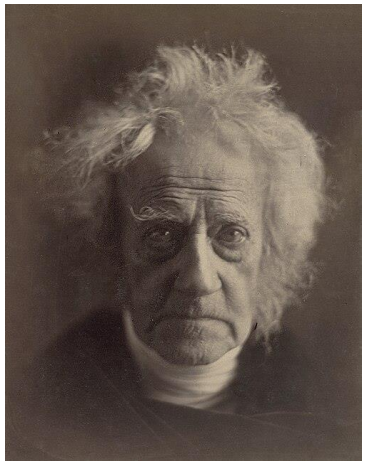
Darwin opens *On the Origin of Species* with …

Charles Darwin (1809 – 1882)

"*When on board H.M.S. Beagle as naturalist, I was much struck with certain facts in the distribution of the inhabitants of South America, and in the geological relations of the present to the past inhabitants of that continent. These facts seemed to me to throw some light on the origin of species– that mystery of mysteries, as it has been called by one of our greatest philosophers.*"

On the Origin of Species (1859)



John Herschel (1792 – 1871)

"*Of course I allude to that mystery of mysteries, the replacement of extinct species by others.*"

Herschel, in appreciation of Lyell's *Principles of Geology* (1836)

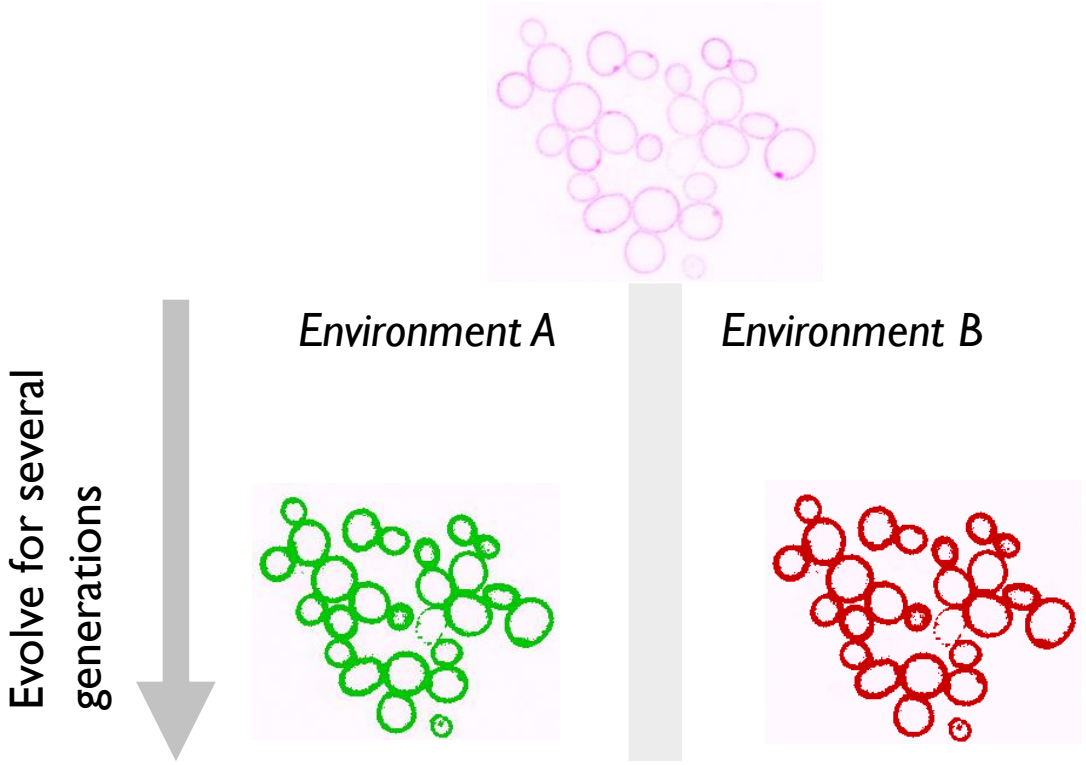
"*heard by round about channel that Herschel says my Book is the law of higgledy-piggledy. What this exactly means I do not know, but it is evidently very contemptuous. If true, this is great blow & discouragement.*"

Darwin's Letter to Charles Lyell (11 Dec 1859)

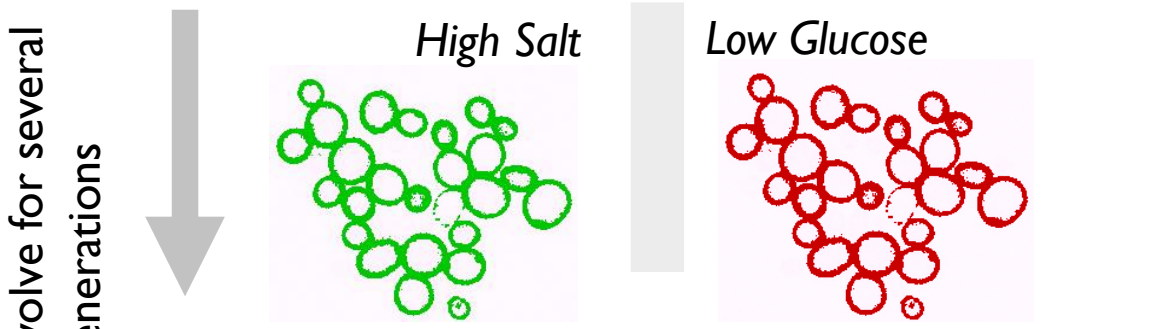
(www.darwinproject.co.uk)

Two extreme modes of speciation.

I. Allopatric speciation. The *null* model of speciation.

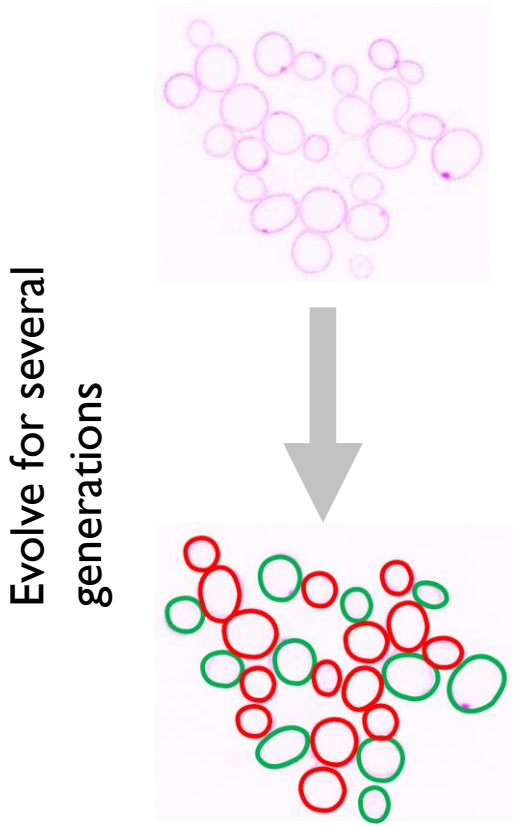


Example from laboratory.



(Dettman et al, 2007, *Nature*)

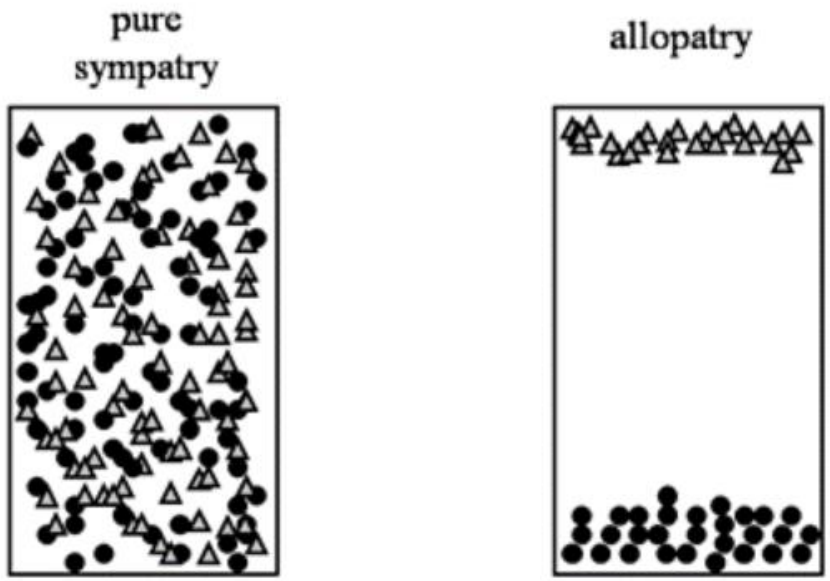
Two extreme modes of speciation.
II. Sympatric speciation. The *"ugly duckling"* of speciation.



Speciation despite members of population allowed to exchange genes with each other.

(Via, *Trends in Ecology and Evolution*, 2001)

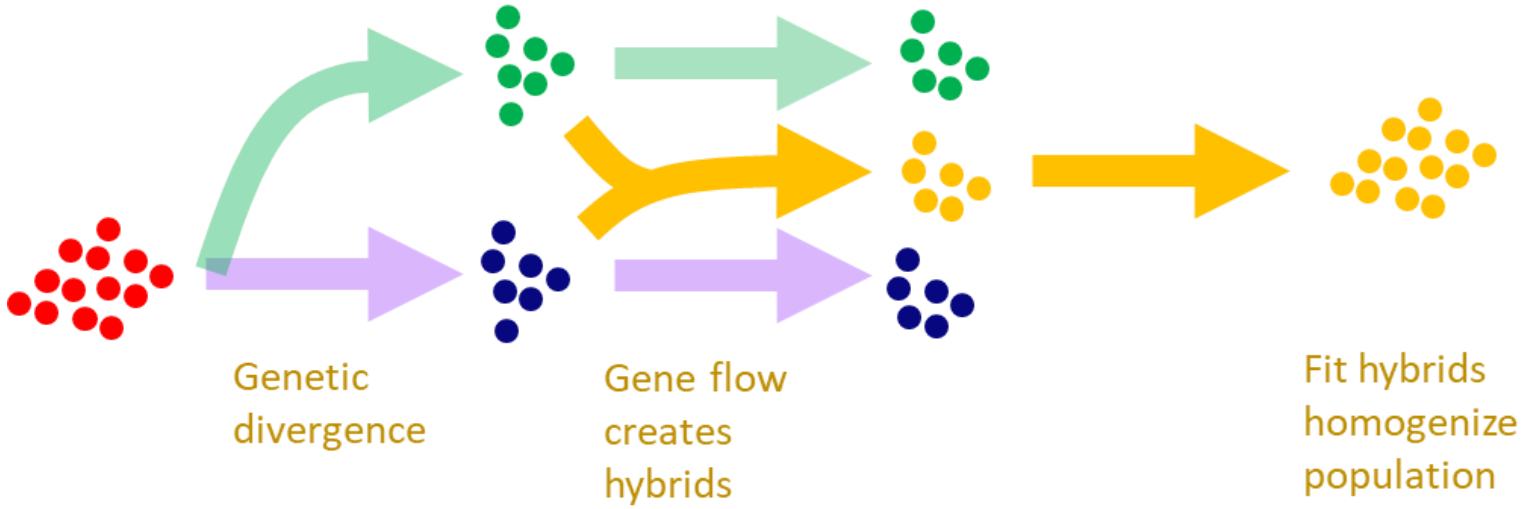
These extremes are end points of a continuum.



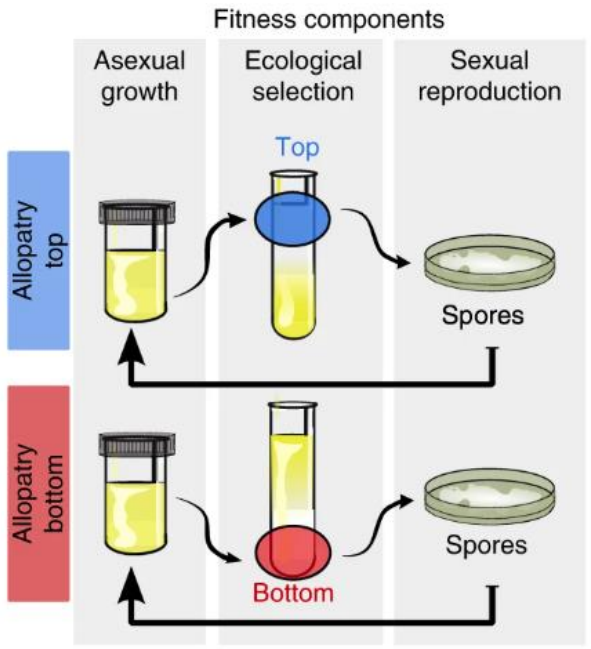
Resistance to gene flow

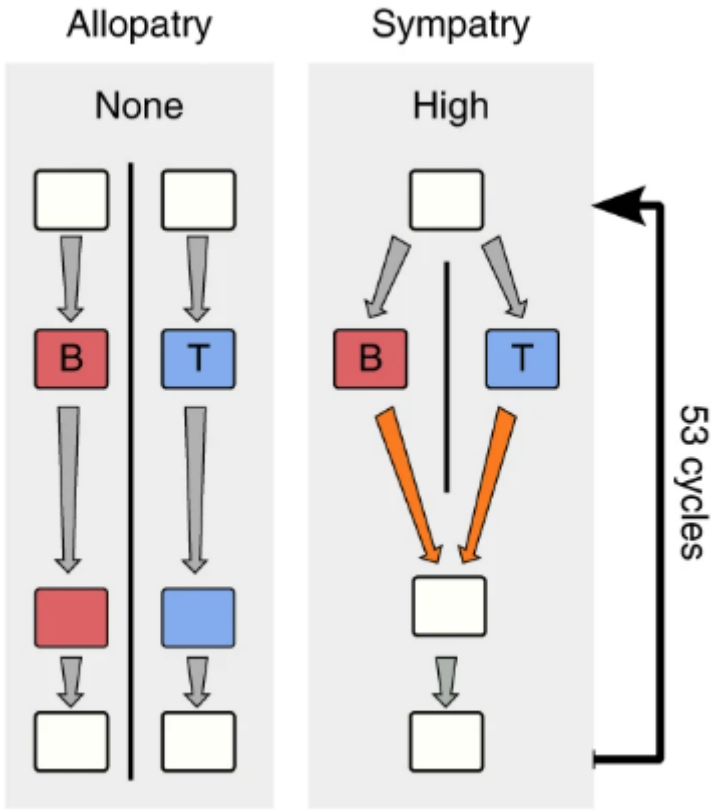
(Mallet et al, 2009, *J. Evolutionary Biology*)
(Fitzpatrick et al, 2008, *J. Evolutionary Biology*)

Gene flow: The problem with demonstrating sympatric speciation



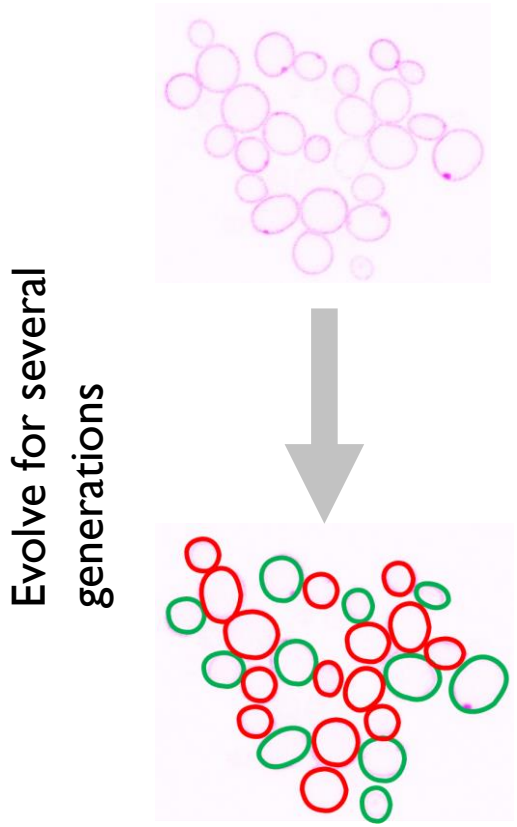
Gene flow is idiosyncratic.



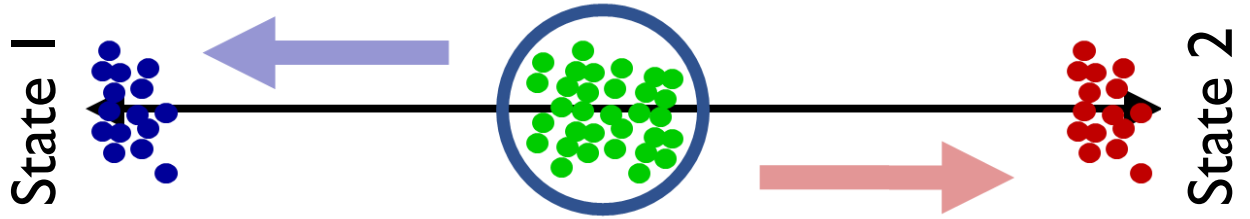


Tusso et al, *NEE*, 2021

For sympatric speciation to occur, we need evolutionary forces that may prevent gene flow or render its product faulty.

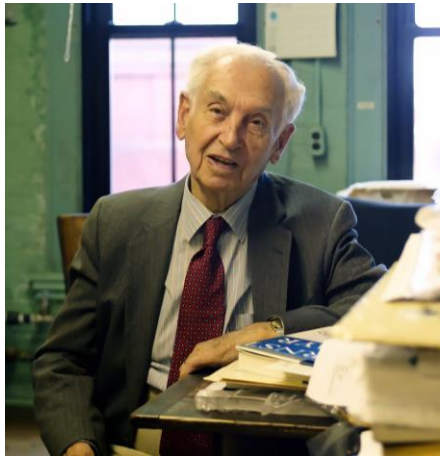


Maintain distinct gene pools and overcome the homogenizing effect of gene flow.



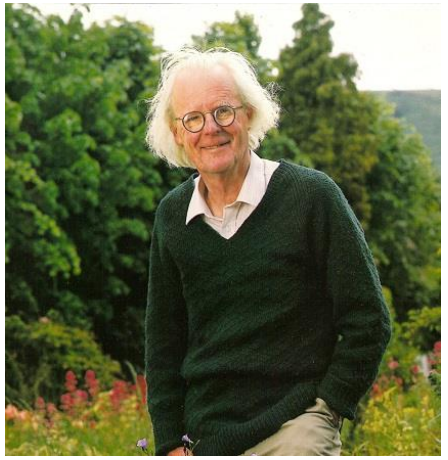
- Disruptive selection
- Sexual selection

Sympatric speciation has had its critics and sympathizers.



"*One would think that it should no longer be necessary to devote much time to this topic, but past experience permits one to predict that the issue will be raised again at regular intervals.*"

- *Animal Species and Evolution,*
Ernst Mayr (1963)

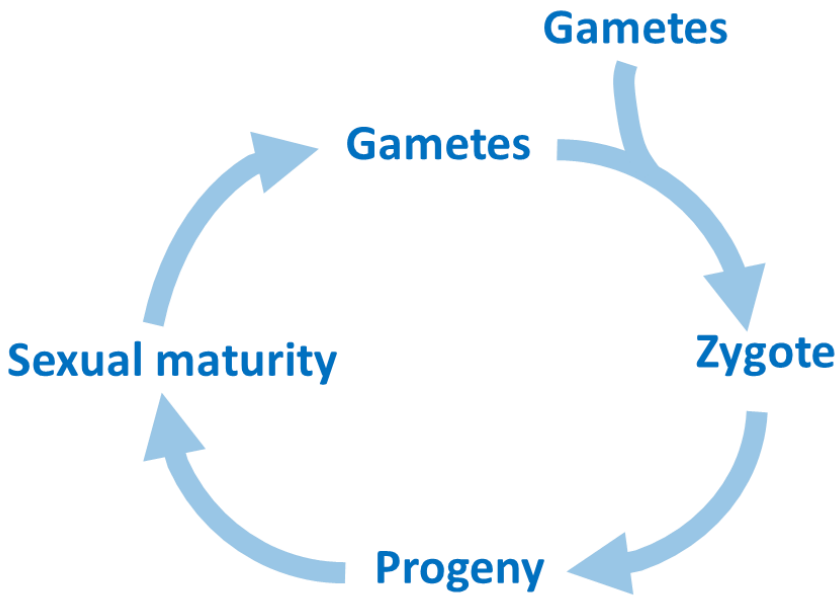


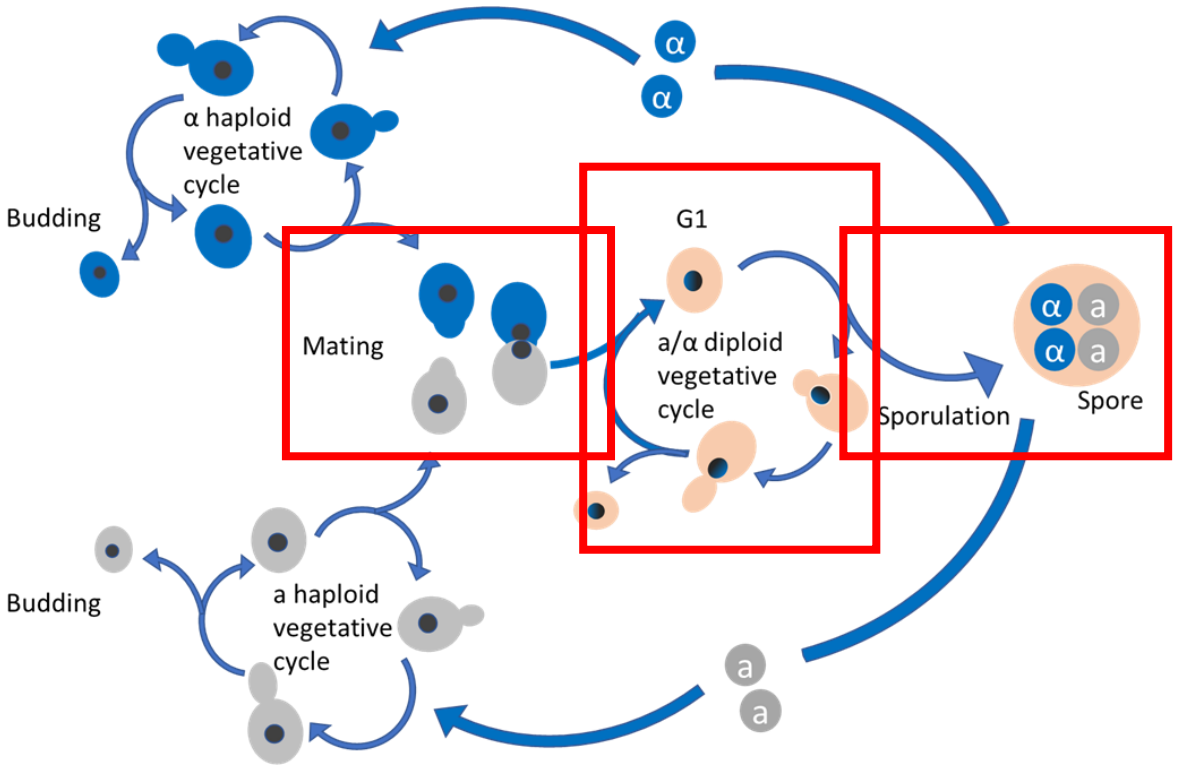
"*The crucial step in sympatric speciation is the establishment of a stable polymorphism in a heterogeneous environment. Whether this paper is regarded as an argument for or against sympatric speciation will depend on how likely such a polymorphism is thought to be*"

John Maynard Smith, *Am. Nat.*, 1966

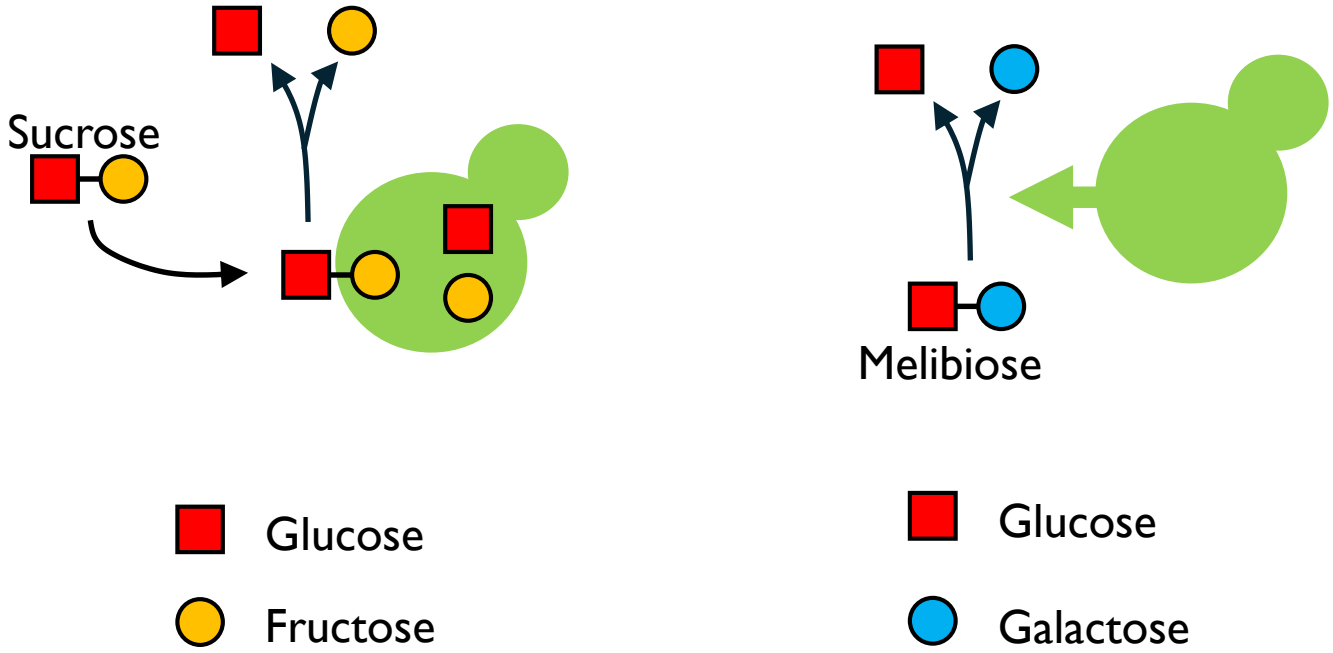
Tauber & Tauber, *Nature* 1977; Kondrashov & Kondrashov, *Nature* 1999; Dieckmann & Doebeli, *Nature* 1999; Higashi et al, *Nature* 1999; Van doorn et al, *Science* 2009; Venkataraman & Saini, npj *Systems Biology and Applications* 2024

Saccharomyces cerevisiae as a model system.



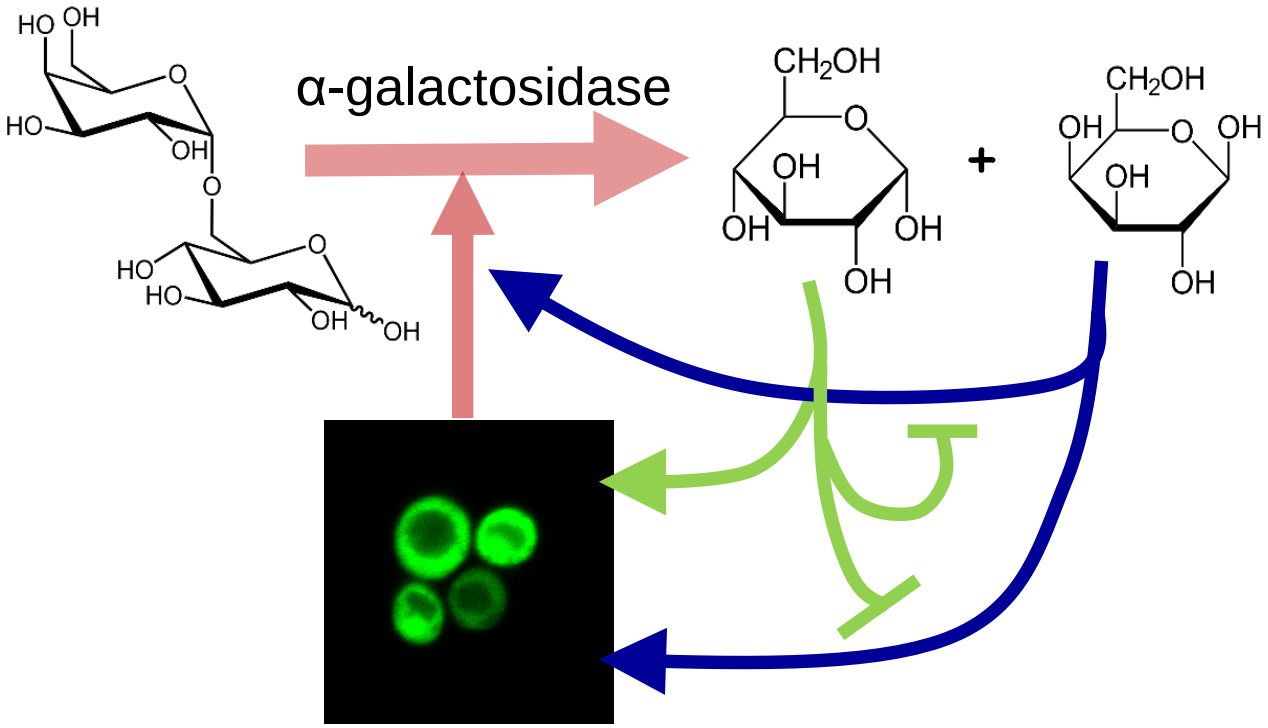


Using public-goods systems to develop models to test likelihood of sympatric speciation.

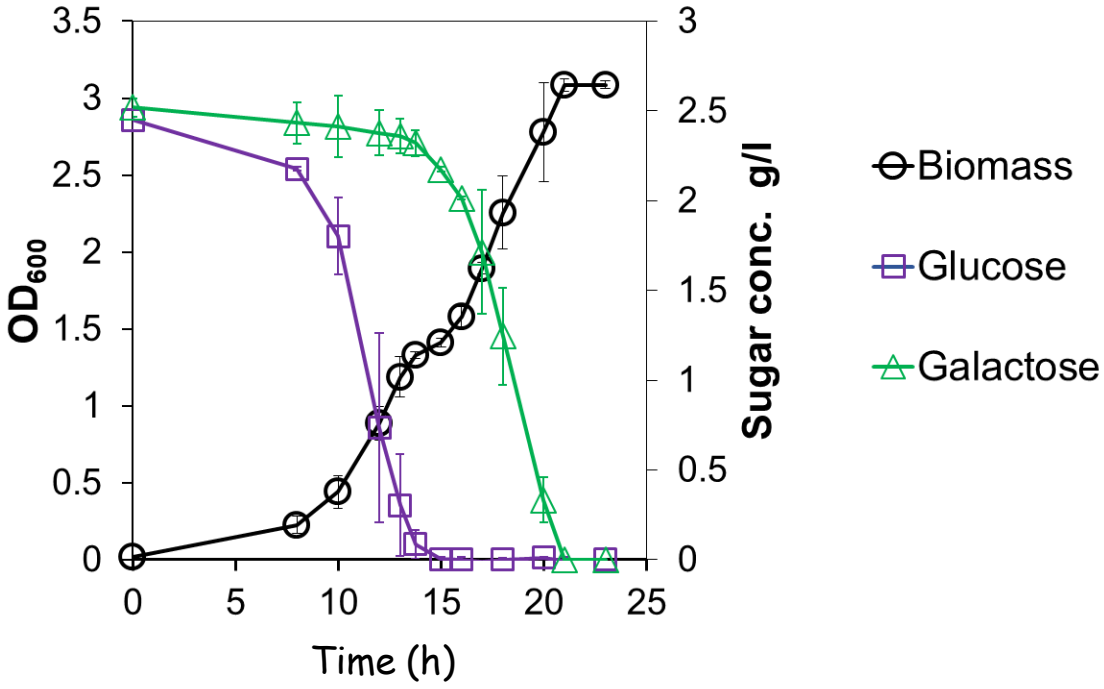


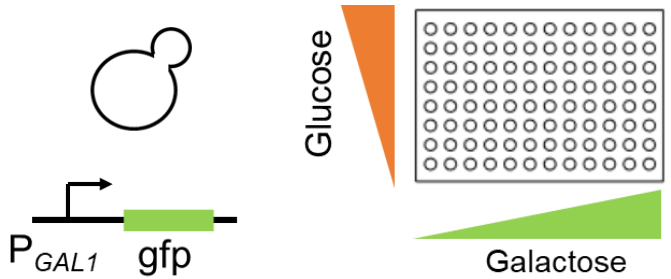
What happens when we evolve yeast populations in these conditions for several hundred generations?

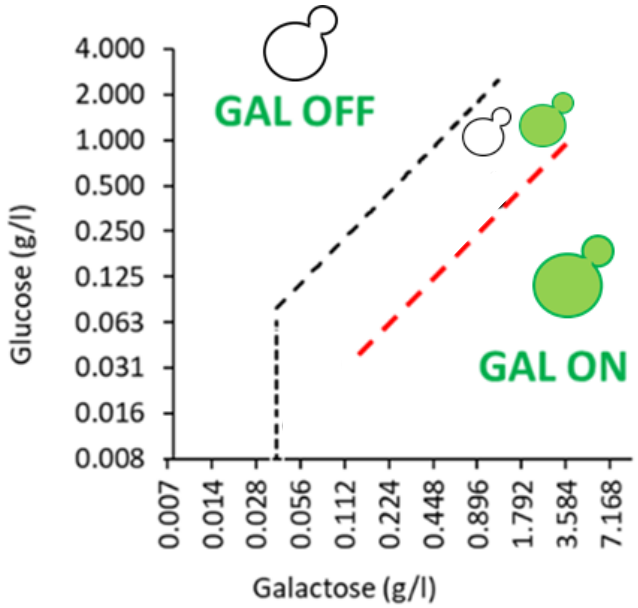
Melibiose utilization system in yeast.



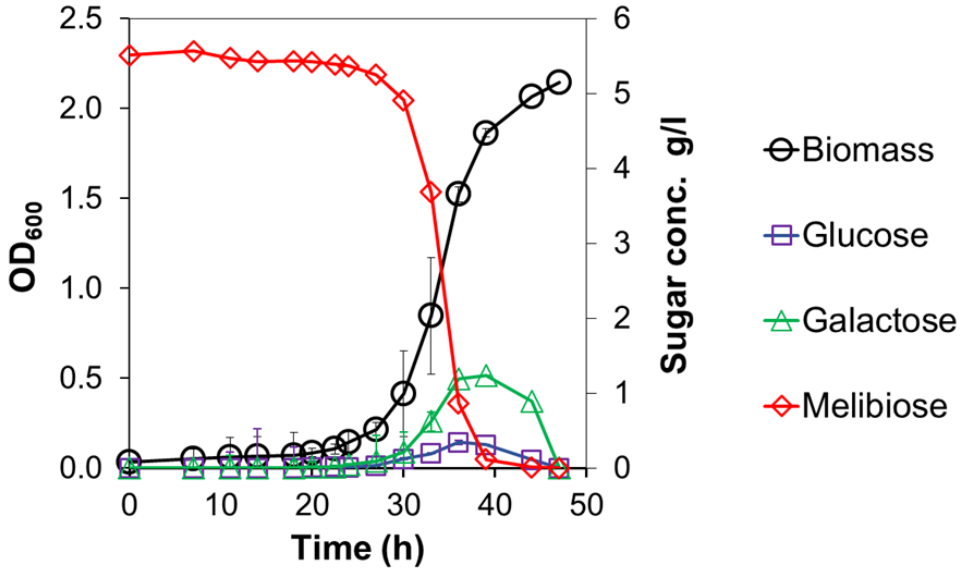
Cellular decision making in a glucose-galactose environment.

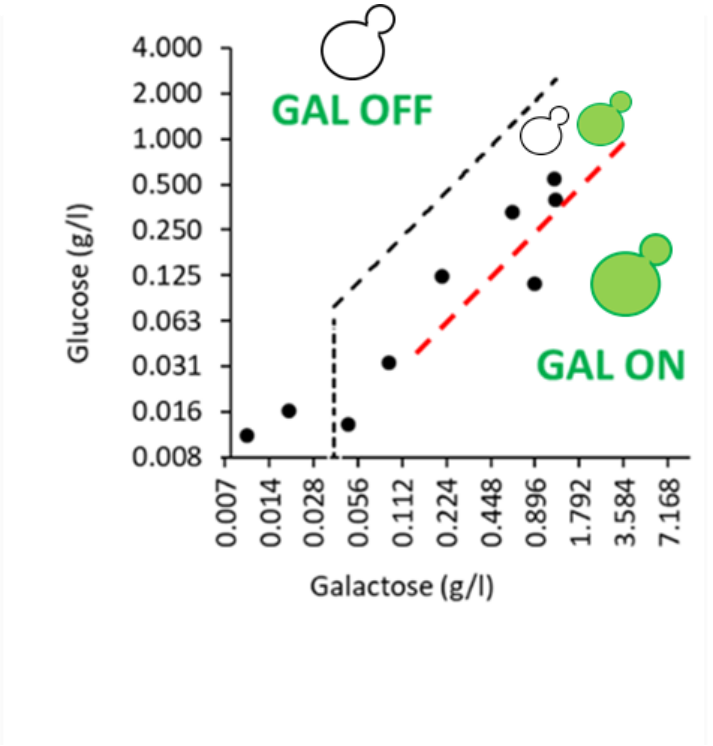




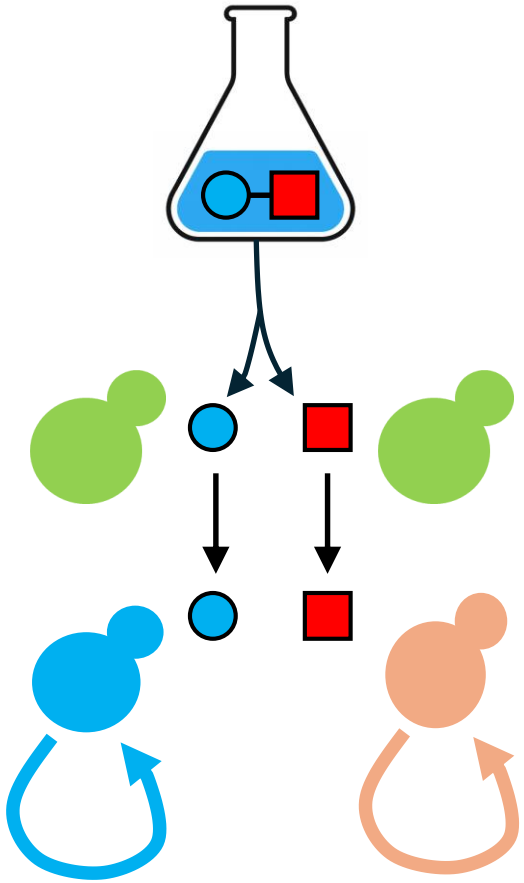


Metabolic heterogeneity during growth on melibiose.

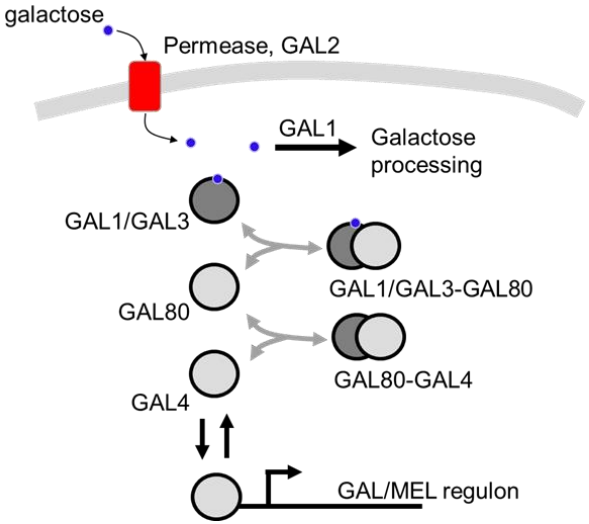


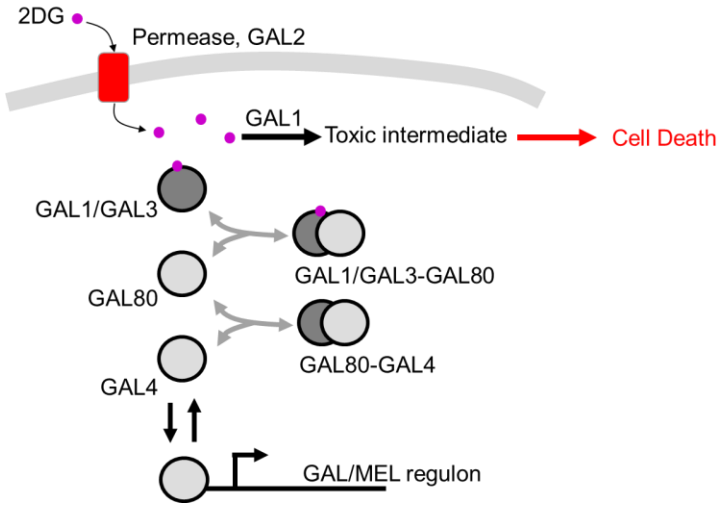


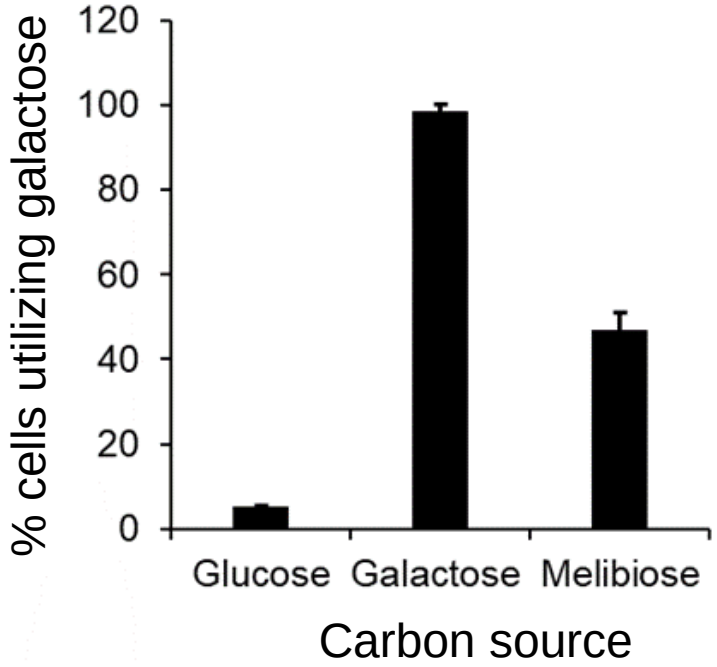
Lessons from using the public-goods driven systems in yeast.

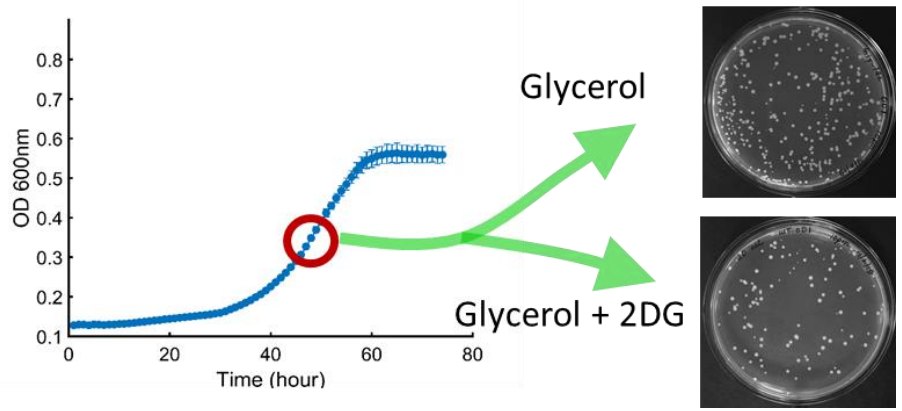


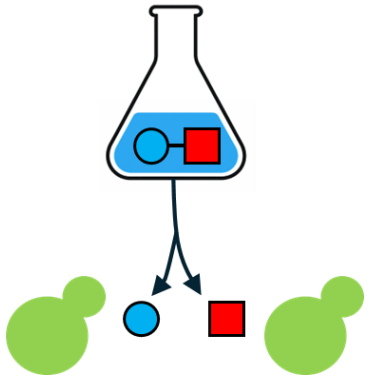
1. An isogenic population exhibits metabolic heterogeneity, when grown on melibiose.





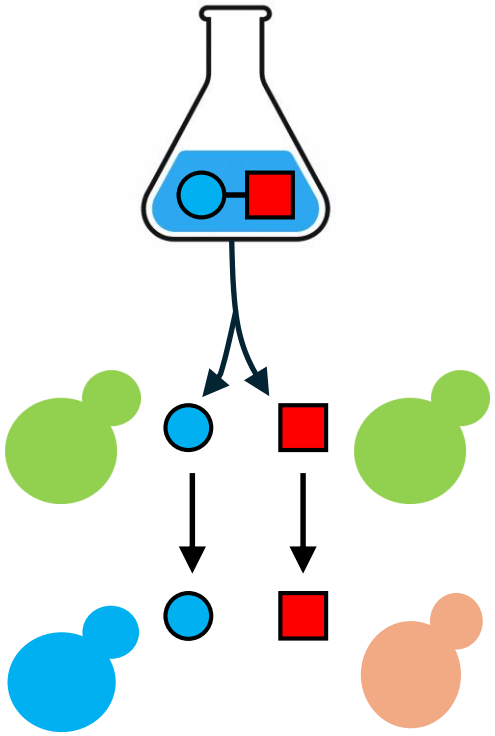






(Mahilkar et al, *Evolution* 2022)

II. When propagated for a few hundred generations, the population splits into two.

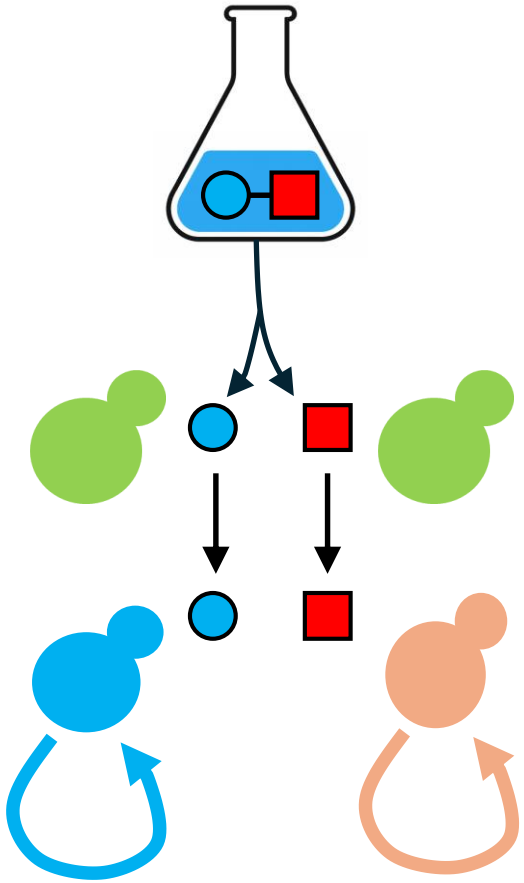


This specialization is driven by single mutational events.

- SNP in GAL3 (melibiose)
- Duplication of sugar transporter (sucrose)

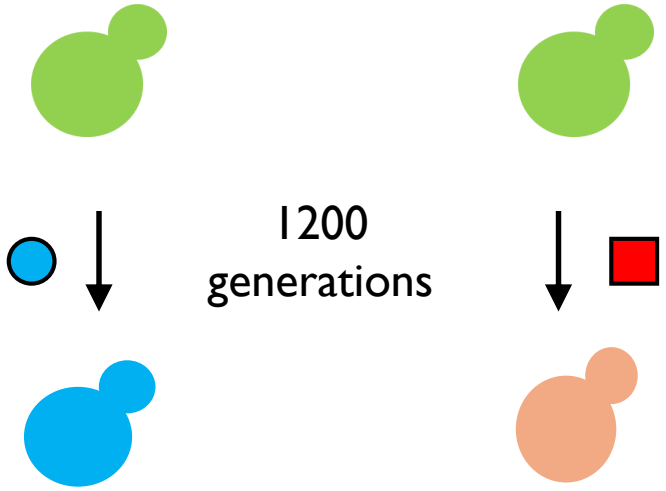
Mahilkar et al, *Evolution* 2022;
Raj & Saini, *Spectrum Microbiology* 2025;
Venkataraman et al, *J. Evolutionary Biology* 2025

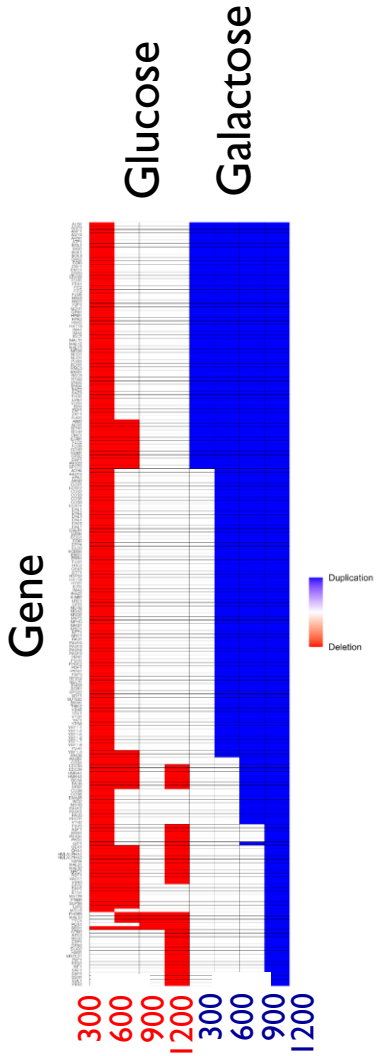
III. Metabolic specialization is linked with assortative mating.



(Mahilkar et al, *Spectrum Microbiology* 2024)

IV. Adaptation on glucose and galactose is driven by opposing deletions and duplications.

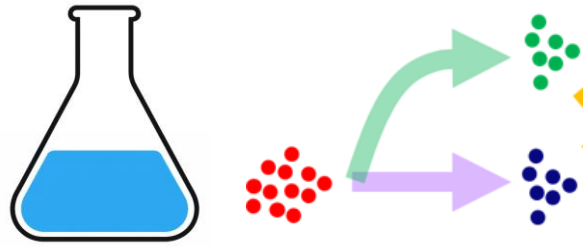




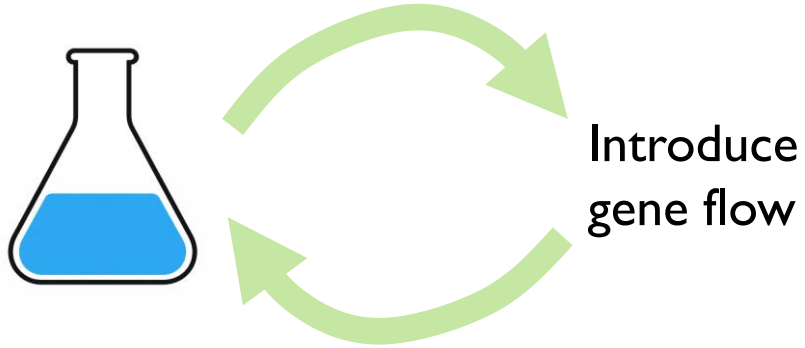
(Nagendra et al, *bioRxiv*, 2025; In Review)

Laboratory evolution experiments with controlled gene flow.

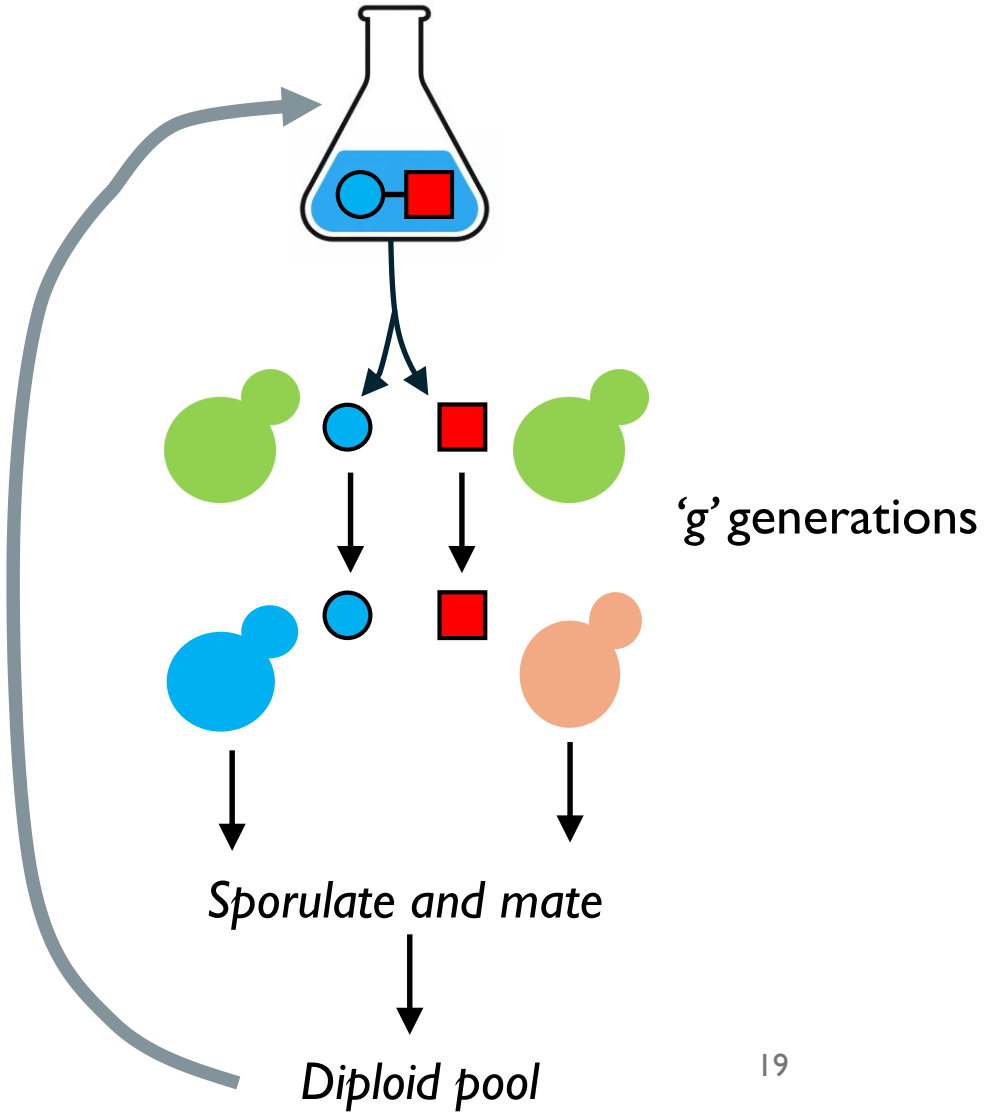
- But this split is not what we seek.



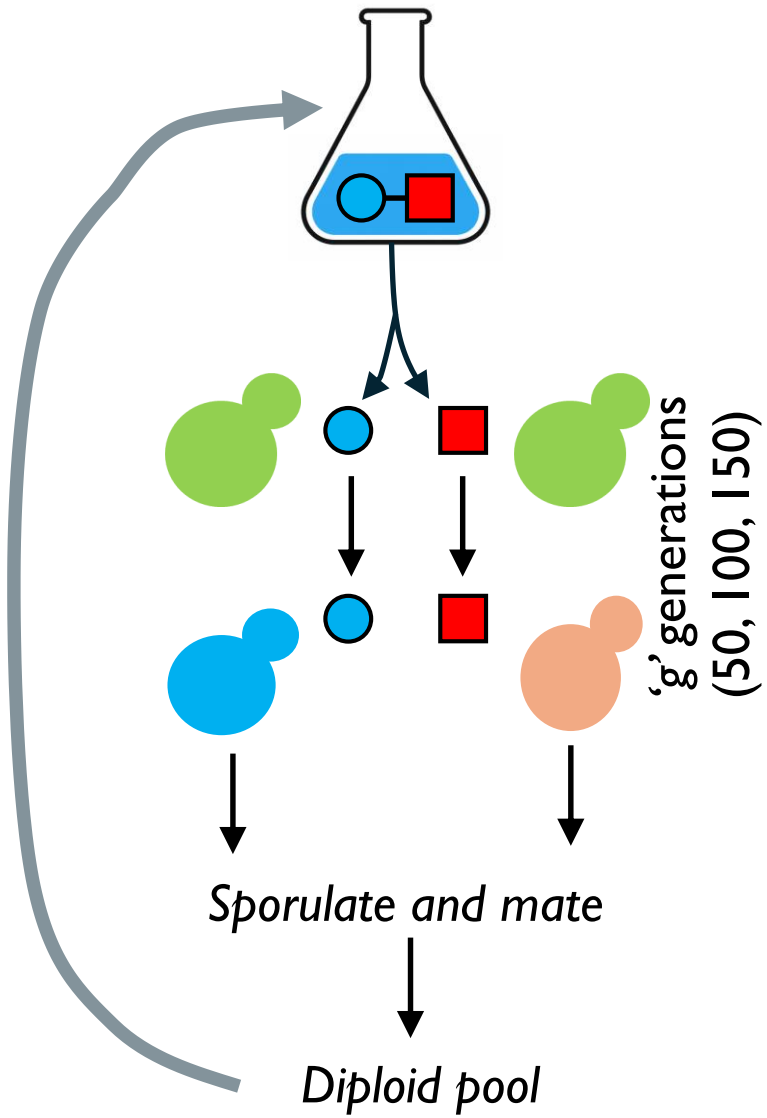
- Introducing gene flow between individuals in the population.

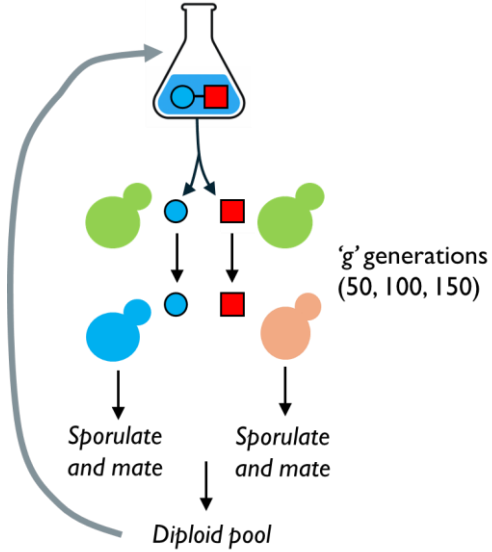


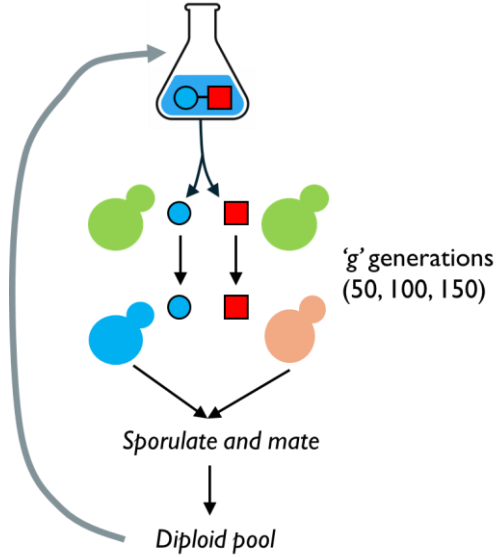
Asexual growth for ‘g’ generations

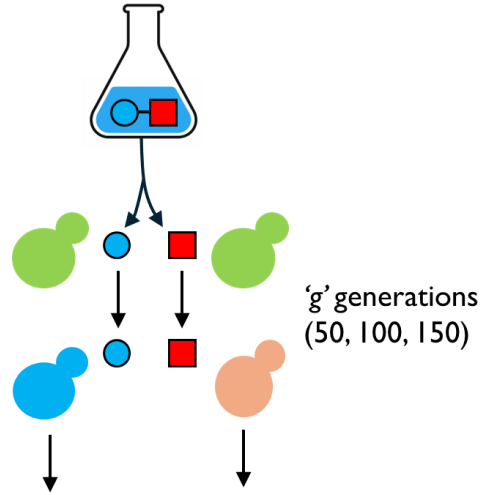


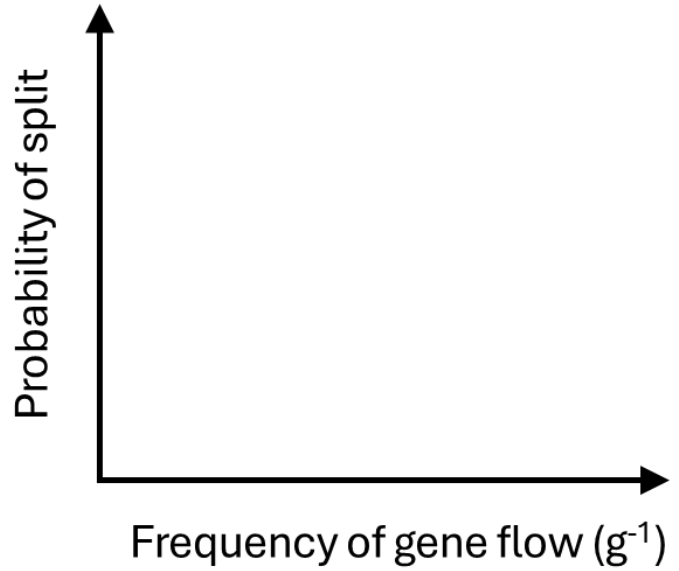
Laboratory evolution experiments with controlled gene flow.











Summary.

Sympatric speciation is an old outstanding problem, an "ugly duckling", in evolutionary biology.

Using yeast and public goods driven systems, we are developing a model system to answer how gene flow impacts adaptive trajectories, and evolution of reproductive isolation.

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