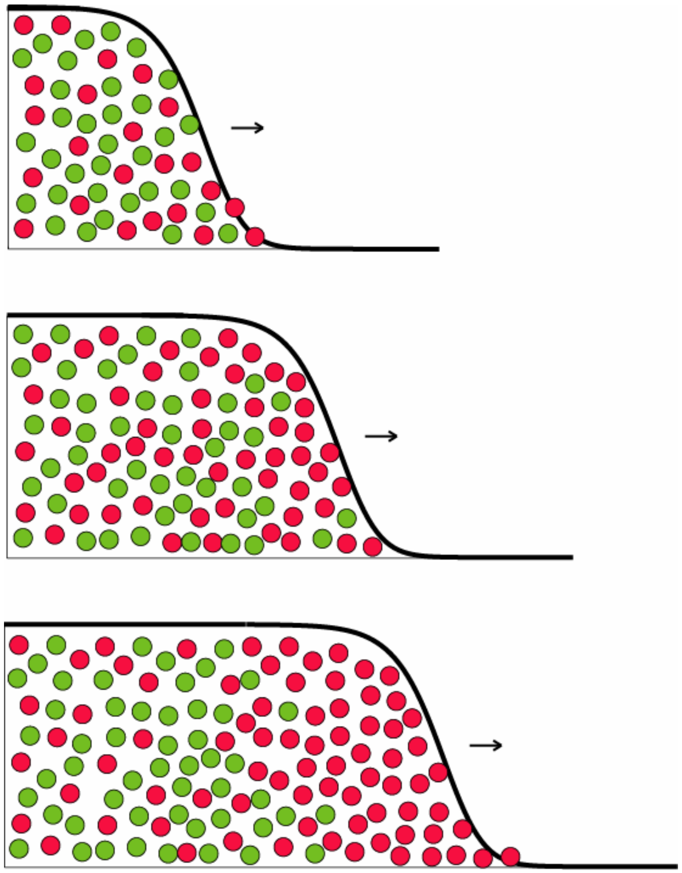
Evolutionary dynamics in spatially structured (as opposed to well-mixed) asexuals.

Oskar Hallatschek

MPI-Dynamics and Self-Organization

Göttingen



http://www.ds.mpg.de/Forschung/index.php

P.h.D. and postdoc positions available!

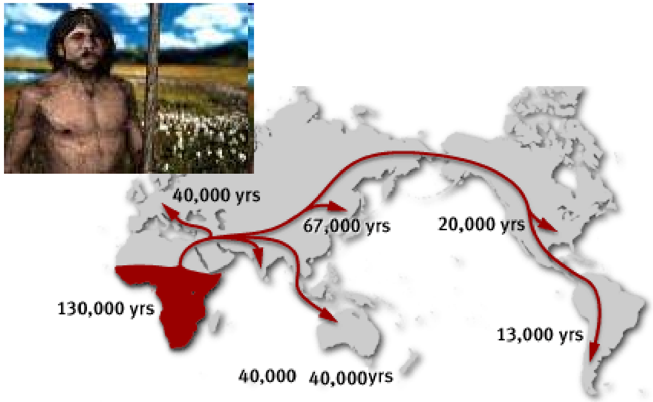
Outline

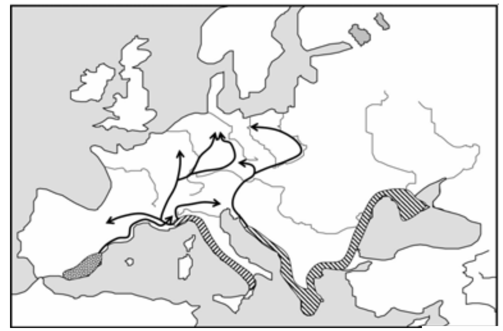
- Neutral drift during range expansions

- Speed of adaptation and genetic load in 1d models

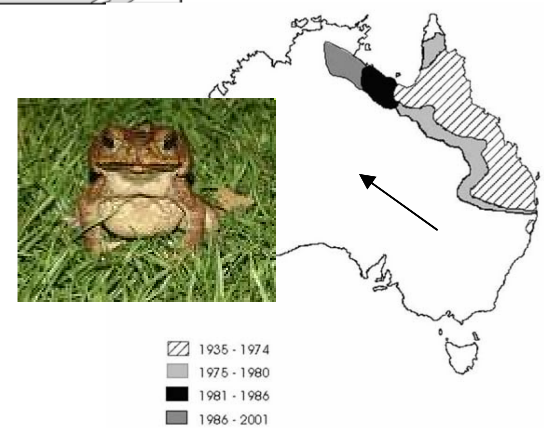
Hill & Robertson

Rang expansions are ubiquitous





Glacial cycles



What is the impact of a range expansion on the gene pool of a population ?

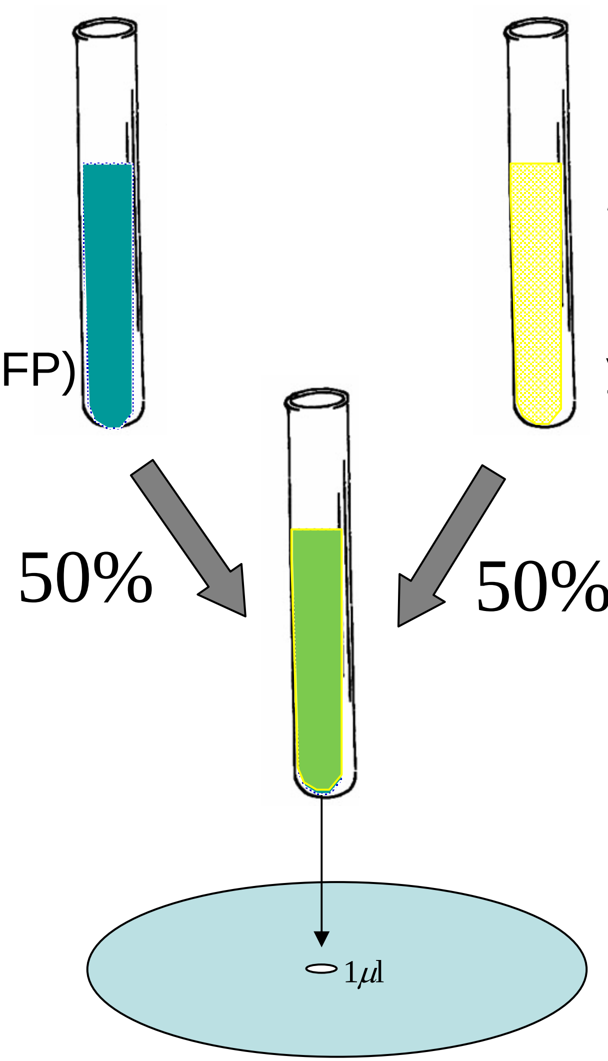
Edmonds, C. A., Lillie, A.S., & Cavalli-Sforza LL. (2004) *PNAS*.

Ramachandran S, Deshpande O, Roseman CC, Rosenberg NA, Feldman MW & Cavalli-Sforza LL. (2005) *PNAS*.

Tracer dynamics in microbial range expansions

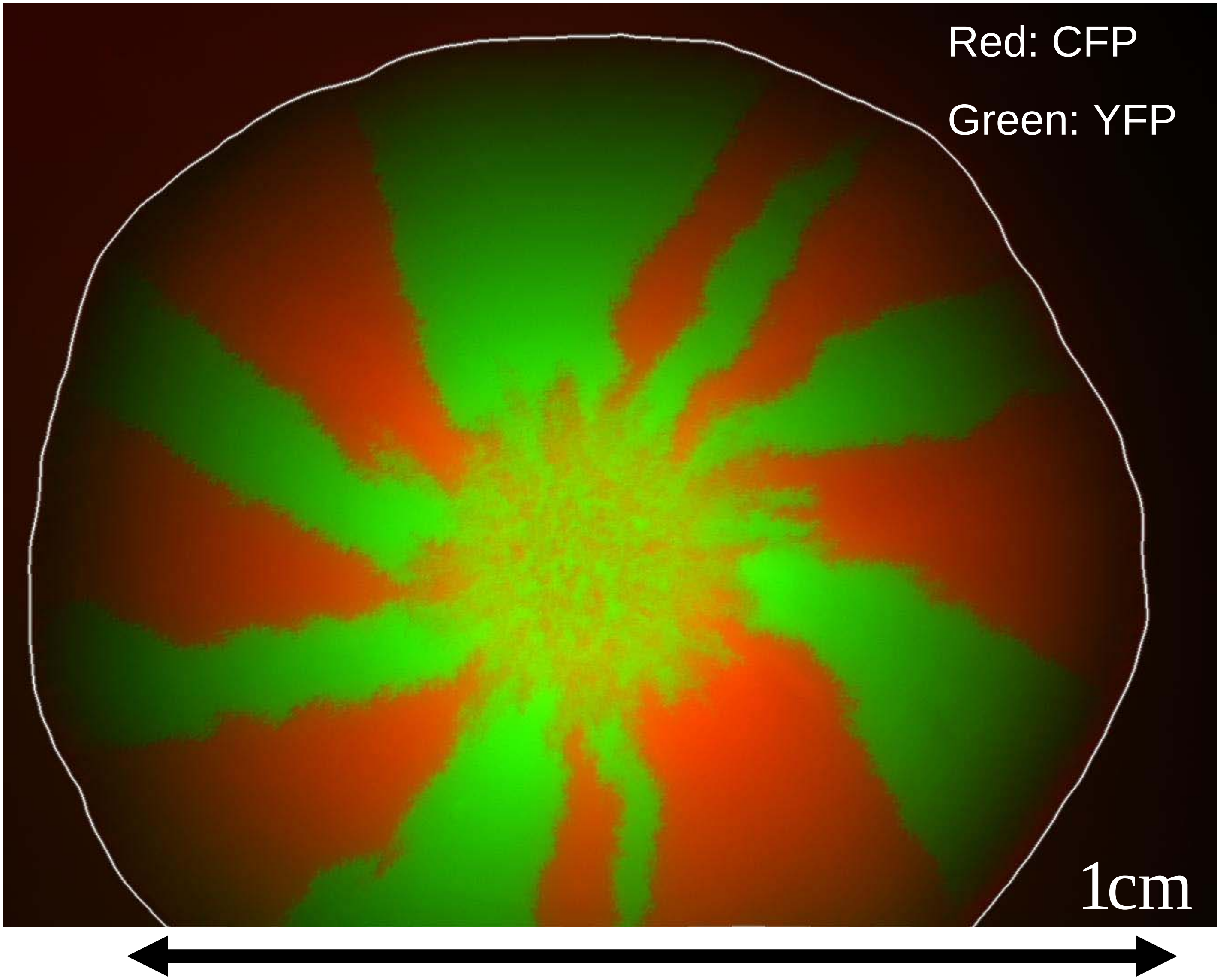
E .coli
labeled
blue (CFP)

E .coli
labeled
yellow (YFP)

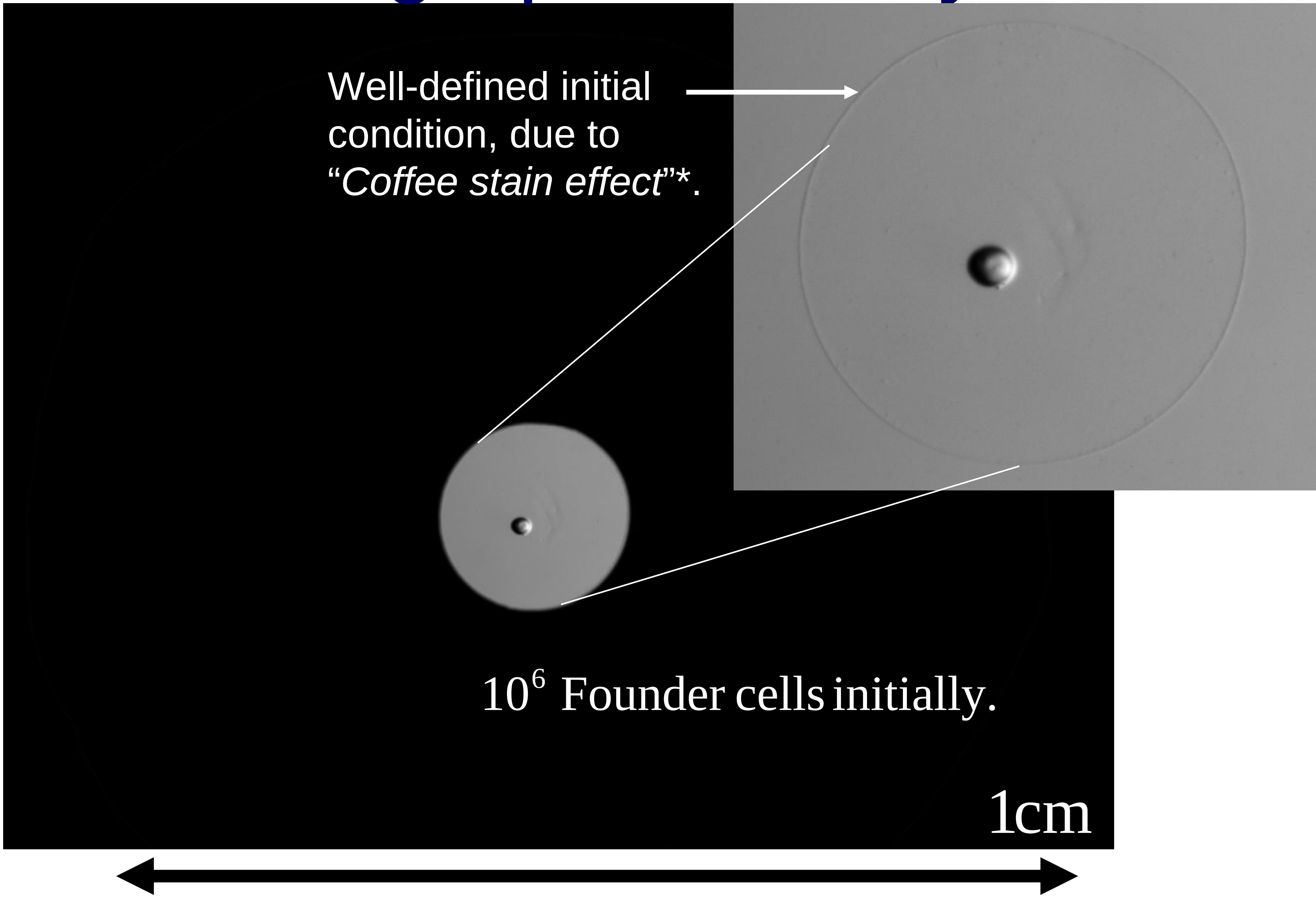


Petri dish with
hard agar and
rich media

Tracer dynamics in E. coli colonies

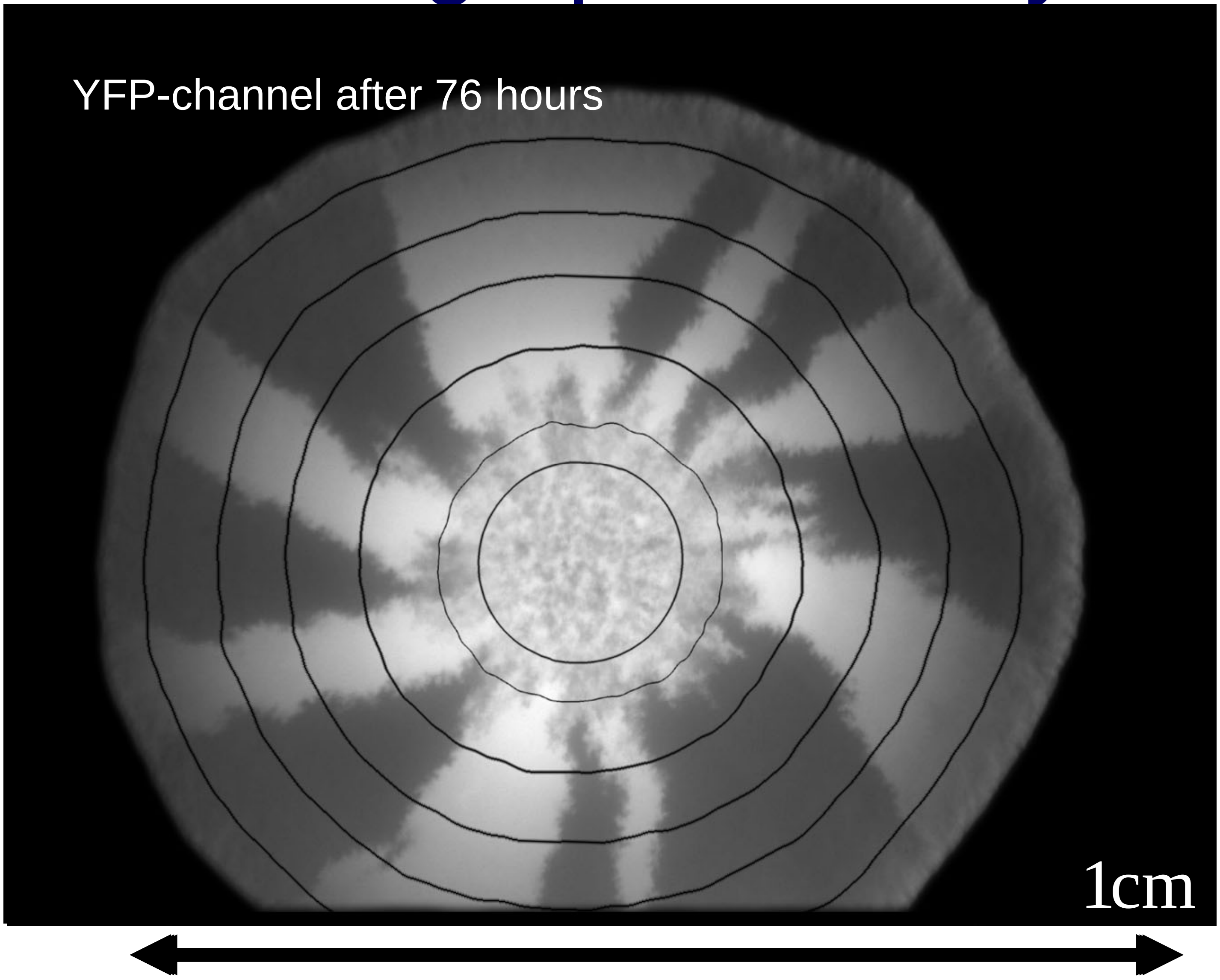


Demographic history

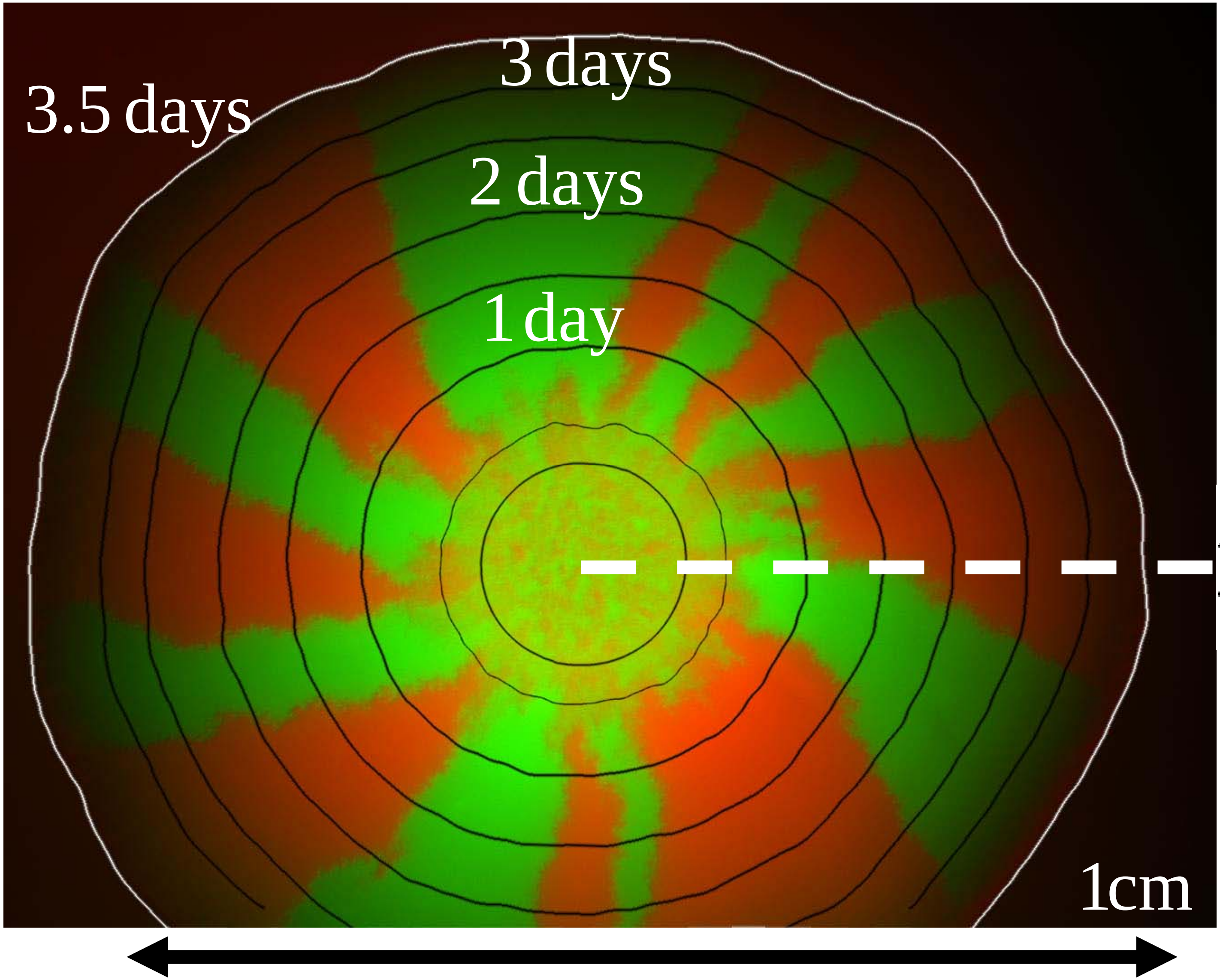


* Deegan RD, Bakajin O, Dupont TF, Huber G, Nagel SR & Witten TA. (1997) Nature 389: 827-829.

Demographic history



Marker diversity in E. coli colonies

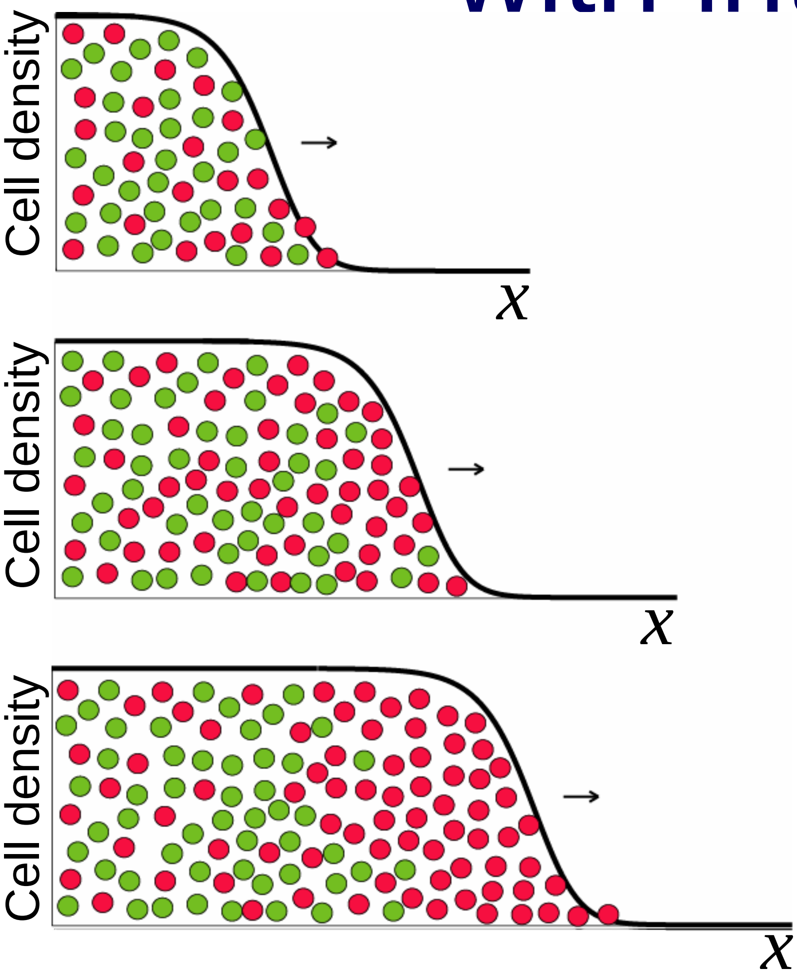


Red: CFP

Green: YFP

O. H., P. Hersen, S. Ramanathan, David R. Nelson (2007) PNAS 104, 19926-19930

Density waves with internal states



$$\partial_t c(x,t) = D\Delta c + s\left(1-\frac{c}{K}\right)c \text{ +noise!}$$

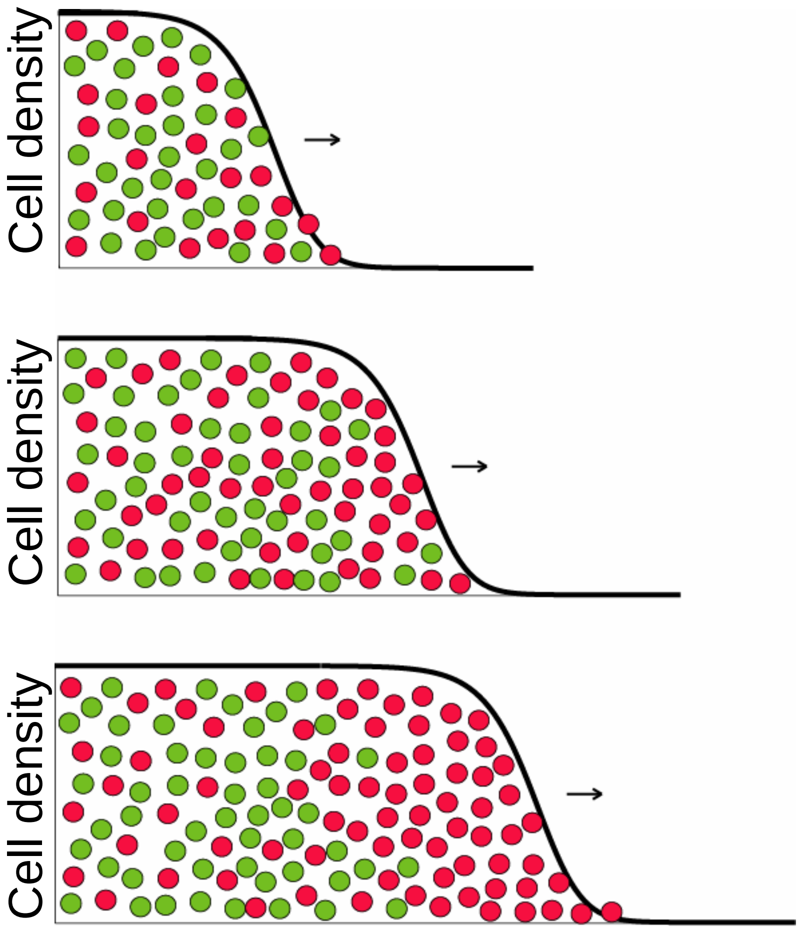
$$\text{velocity} = 2\sqrt{Ds}\times\left\{1-O\left(\ln^{-2}K\right)\right\}$$

R. A. Fisher (1937)

E. Brunet, B. Derrida (1997)

O. H., David R. Nelson (2008) ***Theoretical Population Biology*** **73, 158-170**

Number fluctuations cause demixing in 1d



Mixed initial condition

Number fluctuations

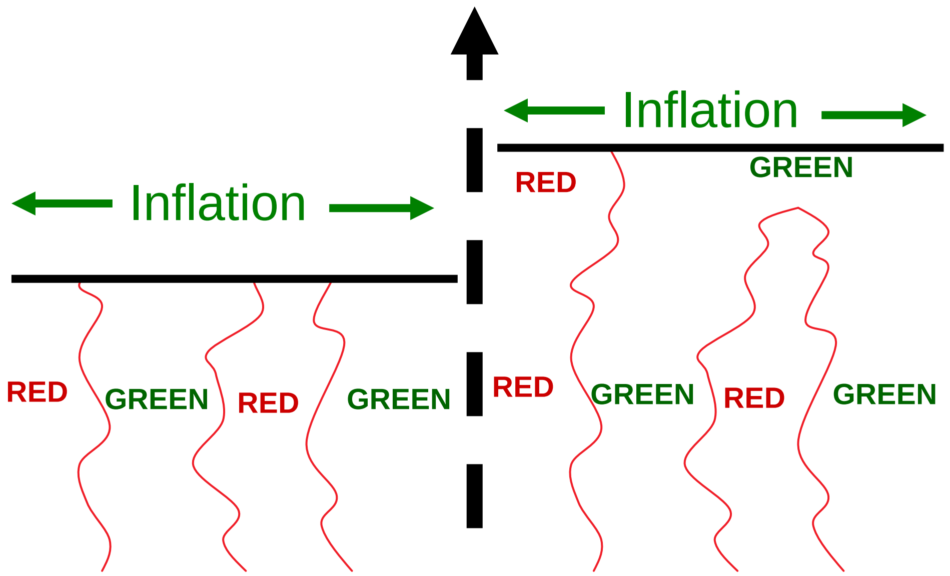
Demixed frontier

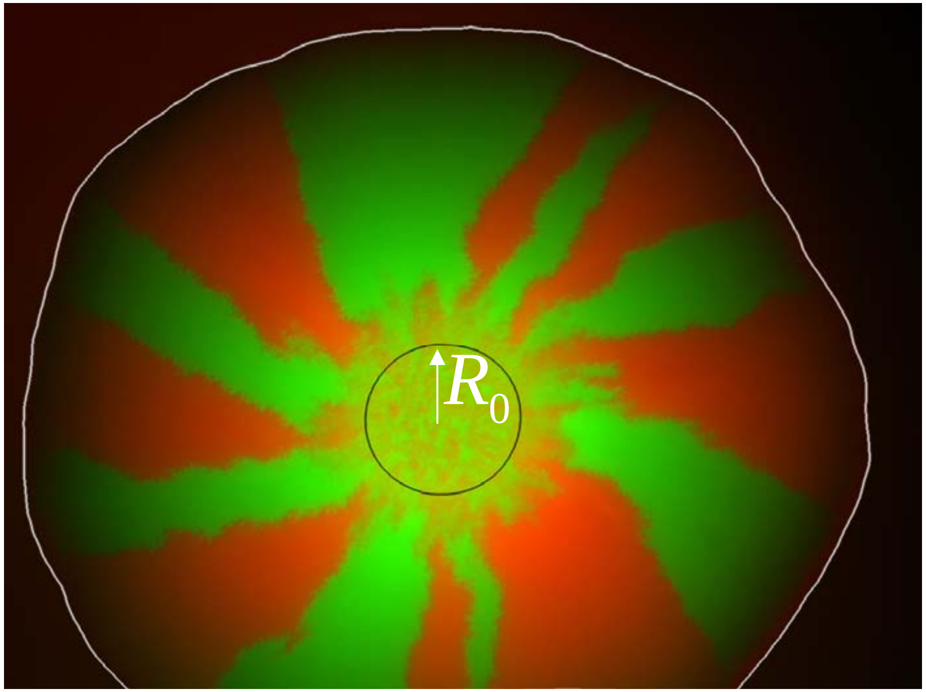
= absorbing state

$$T_{\text{fixation}} = O\left(\ln^{\alpha} K\right)$$

O. H., David R. Nelson (2008) *Theoretical Population Biology* 73, 158-170

Annihilating random walker model with “inflation”



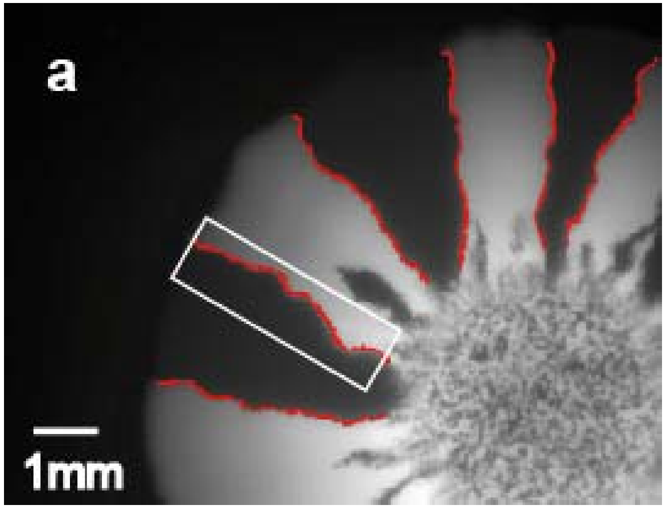


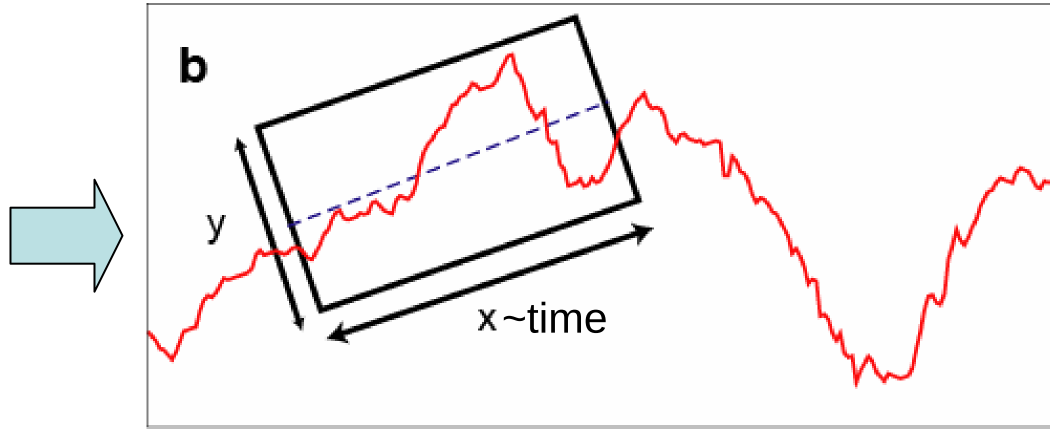
$$t_c \propto R_0$$

$$\langle \#\text{Sectors} \rangle = \sqrt{2\pi R_0 / D_W}$$

… assuming regular diffusion.

Meandering of domain boundaries

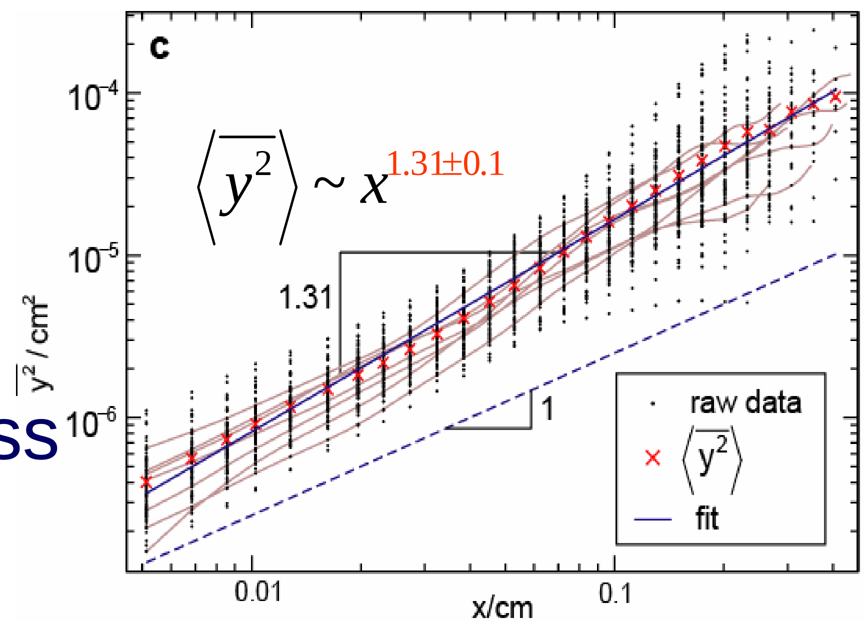




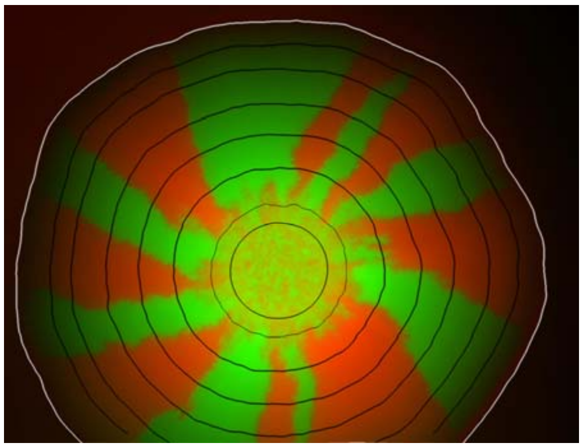
Wandering is superdiffusive!

Why?

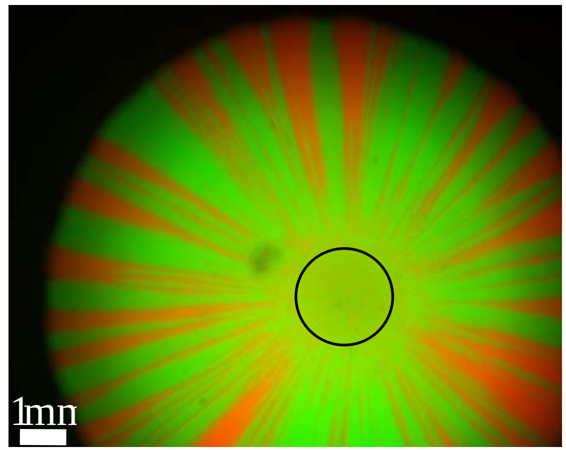
Hypothesis: surface roughness guides wandering $\Rightarrow \left\langle \overline{y^2} \right\rangle \sim x^{4/3}$



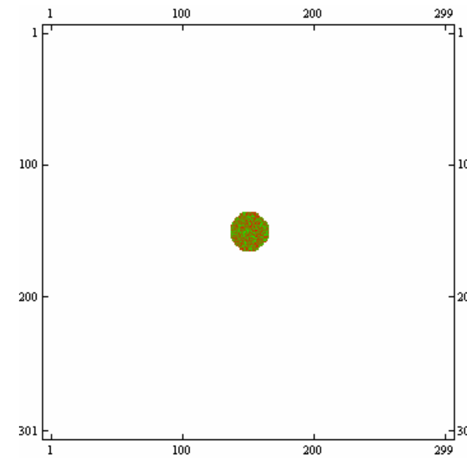
Demixing & coarsening are generic



E. coli



S. Cerevisiae

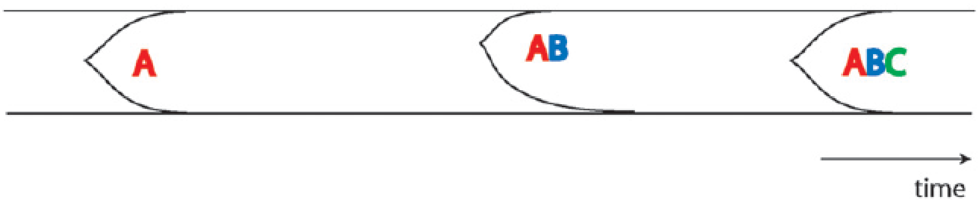


Simulations

Summary:

- Genetic sectoring patterns are characteristic for simple range expansions.
- Can be explained by effects of chance alone.

Speed of adaptation in asexuals – Rep.: The wellmixed case



Periodic selection regime

Beneficial mutations occur at rate NU_b

become established with probability $2s_0$

$$R \equiv \langle \partial_t W \rangle = (NU_b)(2s_0)s_0$$

Fixation time $\log(Ns_0)/s_0 << (2s_0 NU_b)^{-1}$ waiting time

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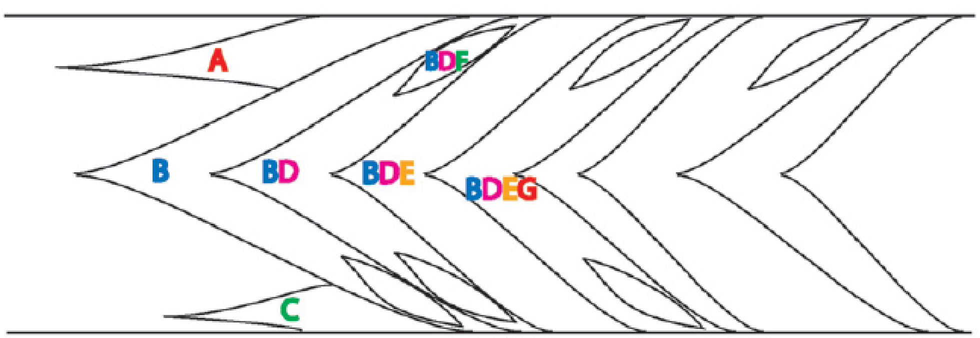


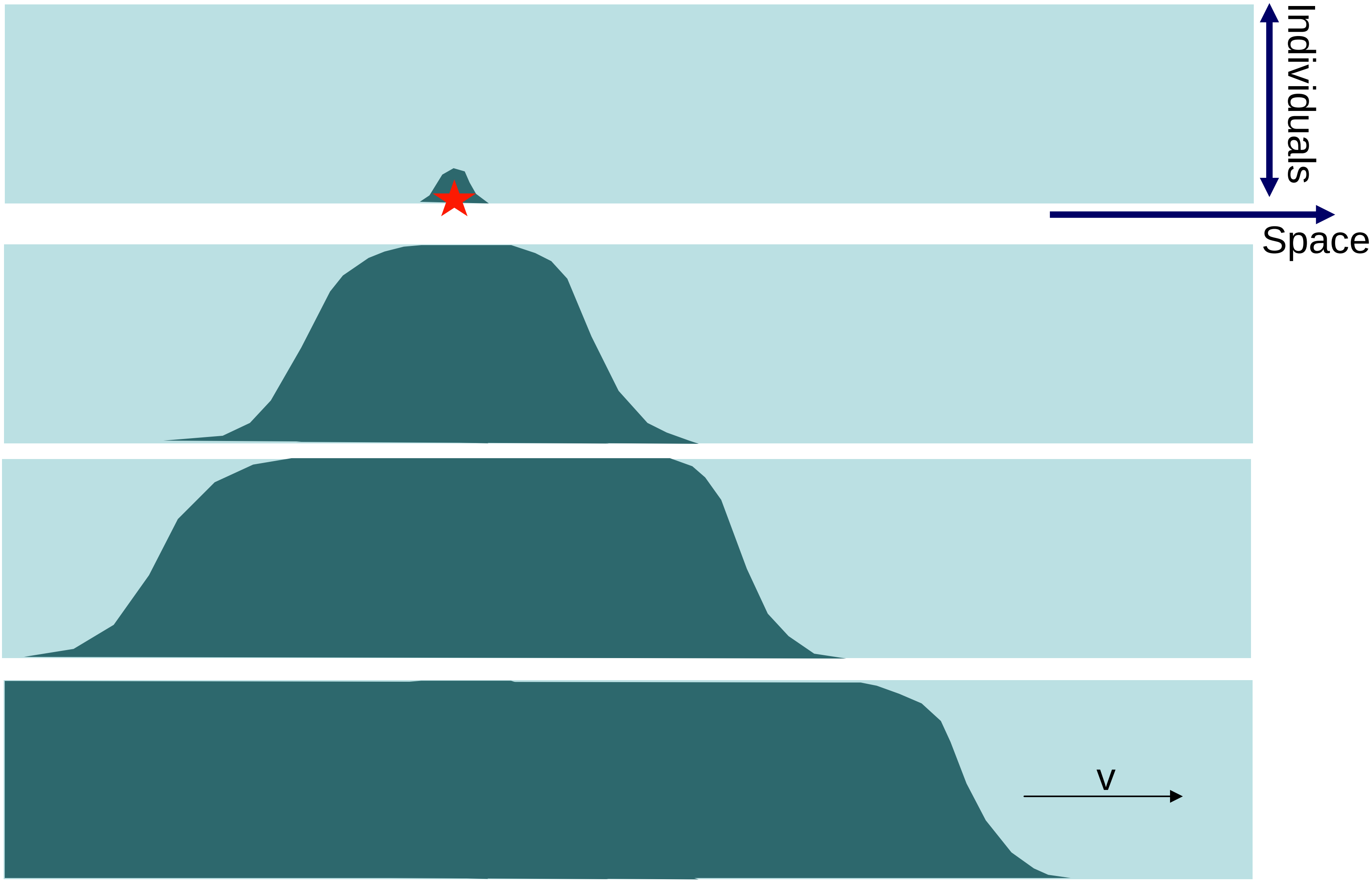
Clonal interference regime

$$R \sim \frac{s_0^2 \ln(N)}{\ln^2(U_b / s_0)}$$

Distribution of fitness effects matters!

Desai, Fisher (2007) Genetics 176, 1759 // Park, Krug (2007) PNAS 140, 18135

Selective sweeps in 1 dimension

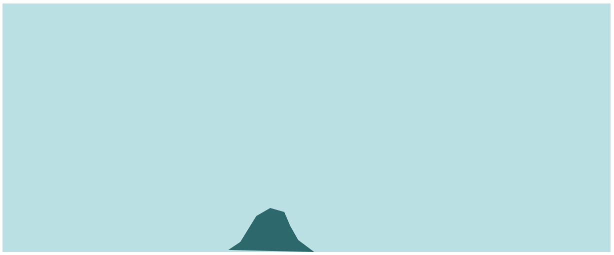


Selective sweeps in 1 dimension

$$\partial_t p(x,t) = D\Delta p + sp(1-p) + \frac{\eta}{K}\sqrt{p(1-p)}$$

Noisy Fisher-Kolmogorov equation

- Establishment probability: $2s$



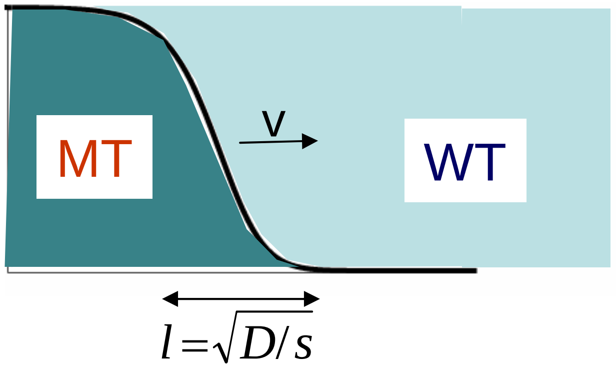
- Wave speed depends on

$$"Ns" \equiv Kls = K\sqrt{D/s}\,s = K\sqrt{Ds}$$

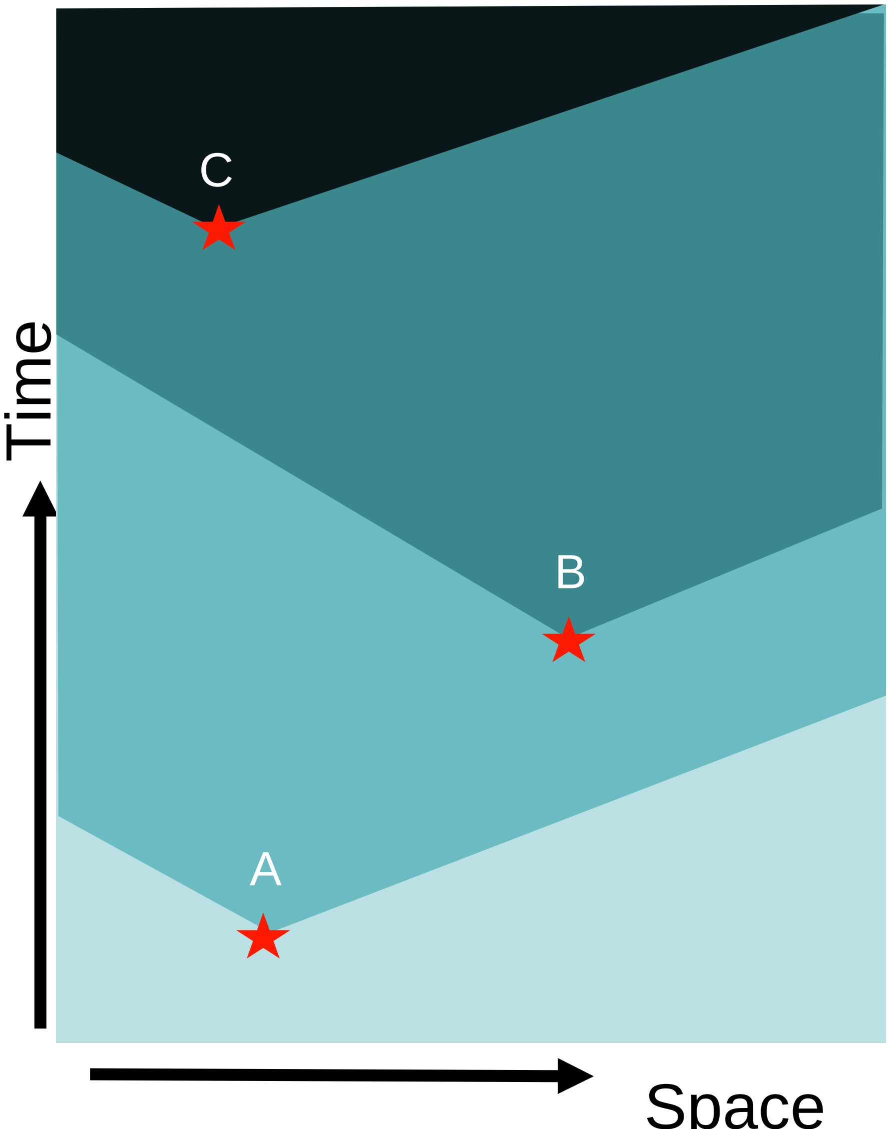
$$\begin{cases} "Ns" \gg 1, \quad \mathrm{v} = 2\sqrt{Ds} \\ "Ns" \ll 1, \quad \mathrm{v} = 2KDs \end{cases}$$

R. A. Fisher (1937) (for $"Ns" \gg 1$)

Doering et al. (2003) (for $"Ns" \ll 1$)



Speed of evolution – $R \equiv \langle \partial_t W \rangle = ?$



Suppose: all new mutations confer the same selective advantage s_0

$$\Rightarrow R_{1D} = NU_b(2s_0)s_0 \overset{!}{=} R_{0D}$$

(periodic selection)

Dimensional analysis:

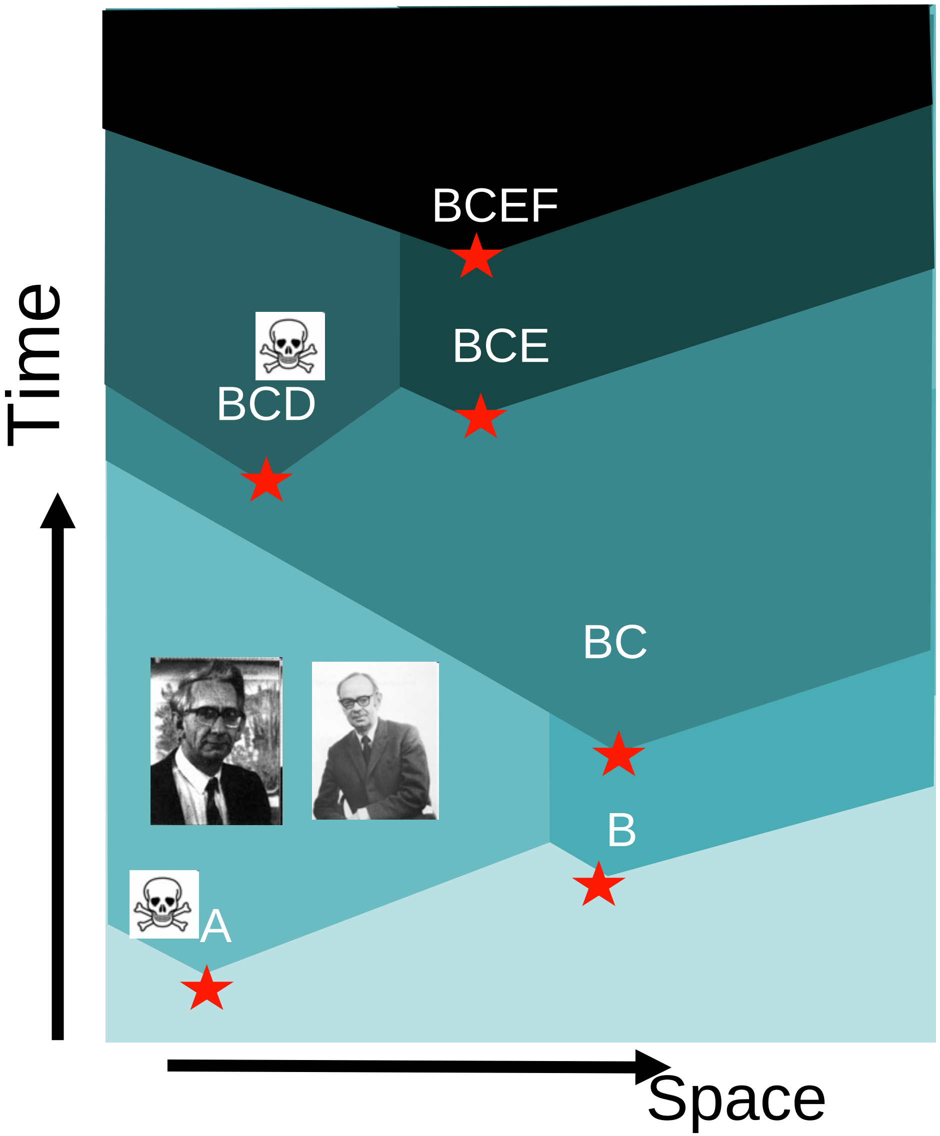
$r \equiv R / s_0 = [T^{-1}]$ can only depend on

$$\mu_b \equiv U_b K(2s_0) \quad [(LT)^{-1}]$$
$$\mathrm{v} \quad [L/T]$$
$$\mathrm{L}_{\mathrm{tot}} \quad [L]$$

Periodic selection for $\mu_b L_{tot} << \mathrm{v}/L_{tot}$

$$r_{1D} = \mu_b L_{tot}$$

Speed of evolution – clonal interference



In general, a fraction F of beneficial mutations is lost by Hill & Robertson.

$$r = L_{tot}\mu_b \; F\left(\frac{L_{tot}}{\sqrt{v/\mu}}\right)$$

<u>Expectation:</u>

$$F(x) \to \begin{cases} 1, \text{ for } x \to 0 \\ \text{const.}/x, \text{ for } x \to \infty \end{cases}$$

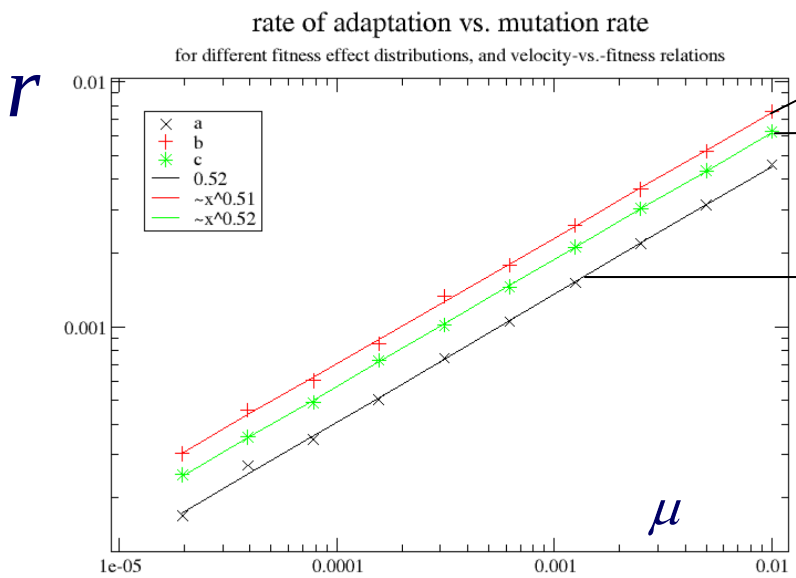
i.e., in the clonal interference regime, we have

$$R_{1D} \sim \sqrt{U_b K v}\, s_0^{3/2}$$

Compare with $R_{0D} \sim \dfrac{s_0^2 \ln(N)}{\ln^2(U_b / s_0)}$

Prähofer, Spohn (2000) PRL, 84, 4882 - 4885

Scaling seems robust



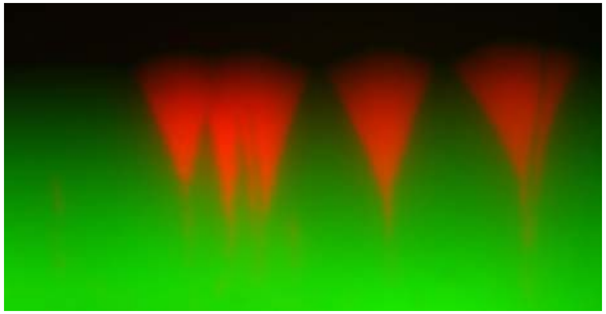
$v \sim s, \quad "Ns" << 1$

$v \sim \sqrt{s}, \quad "Ns" >> 1$

Exponential distribution of fitness effects

The same s_0 for all mutations

- The scaling $R_{1D} \propto \sqrt{U_b K}$ for large systems seems independent of the distribution of fitness-effects and on relation between velocity and fitness advantage!
- generalization to D>1 straight forward.
- could possibly be tested in microbial experiments.



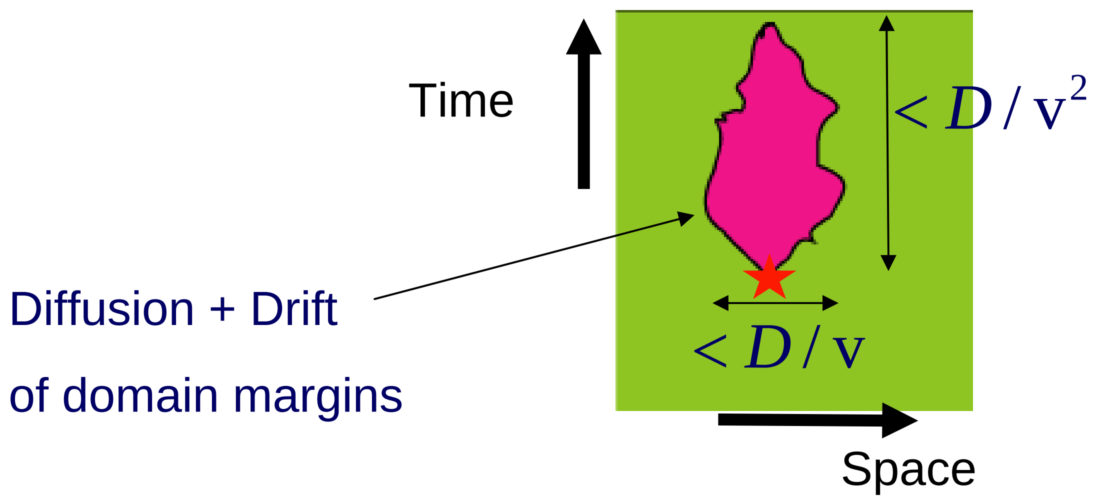
Genetic load

- U_d mutation rate of wildtype into less fit mutant type.
- s selective disadvantage.
- Question: What is the fraction of mutants in equilibrium?

$"Ns" >> 1,$ Deterministic limit → Genetic load is as in the well-mixed case

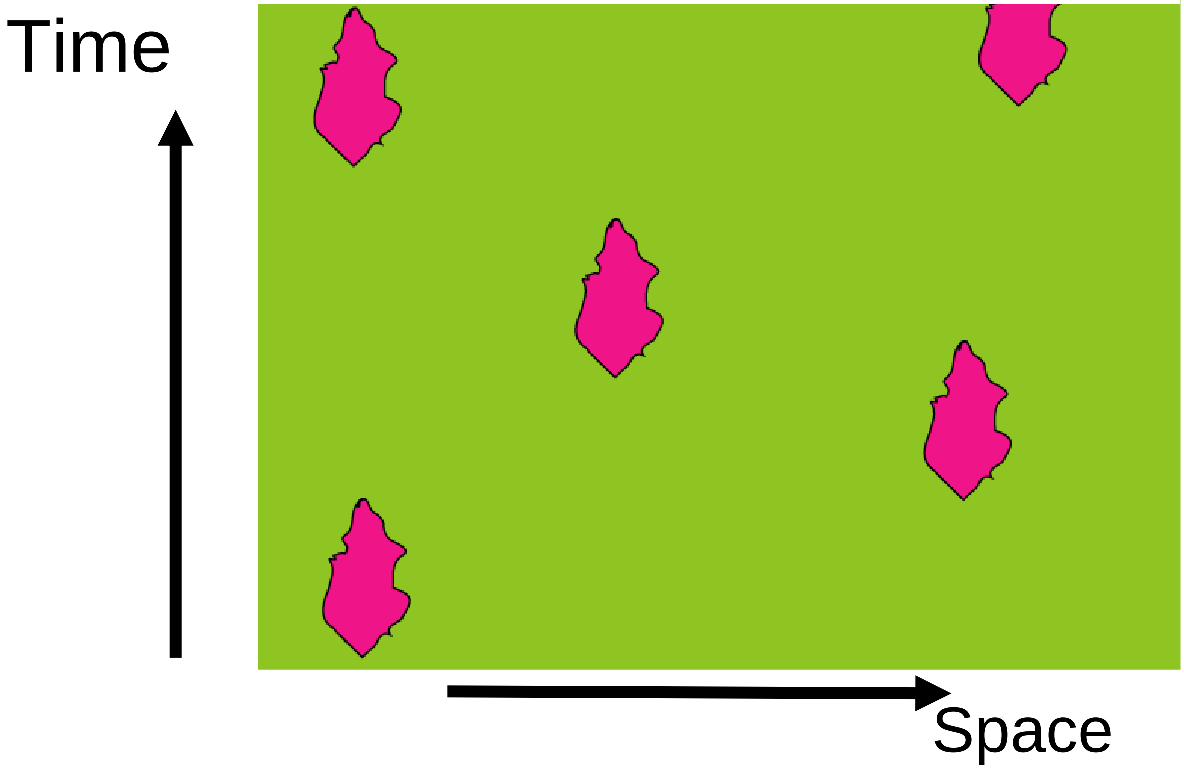
$$\text{i.e., fraction of mutants} \quad q = \frac{U_d}{s}$$

$"Ns" \equiv K\sqrt{Ds} << 1$ Weak selection limit → “bubbles”



$$q = ?$$

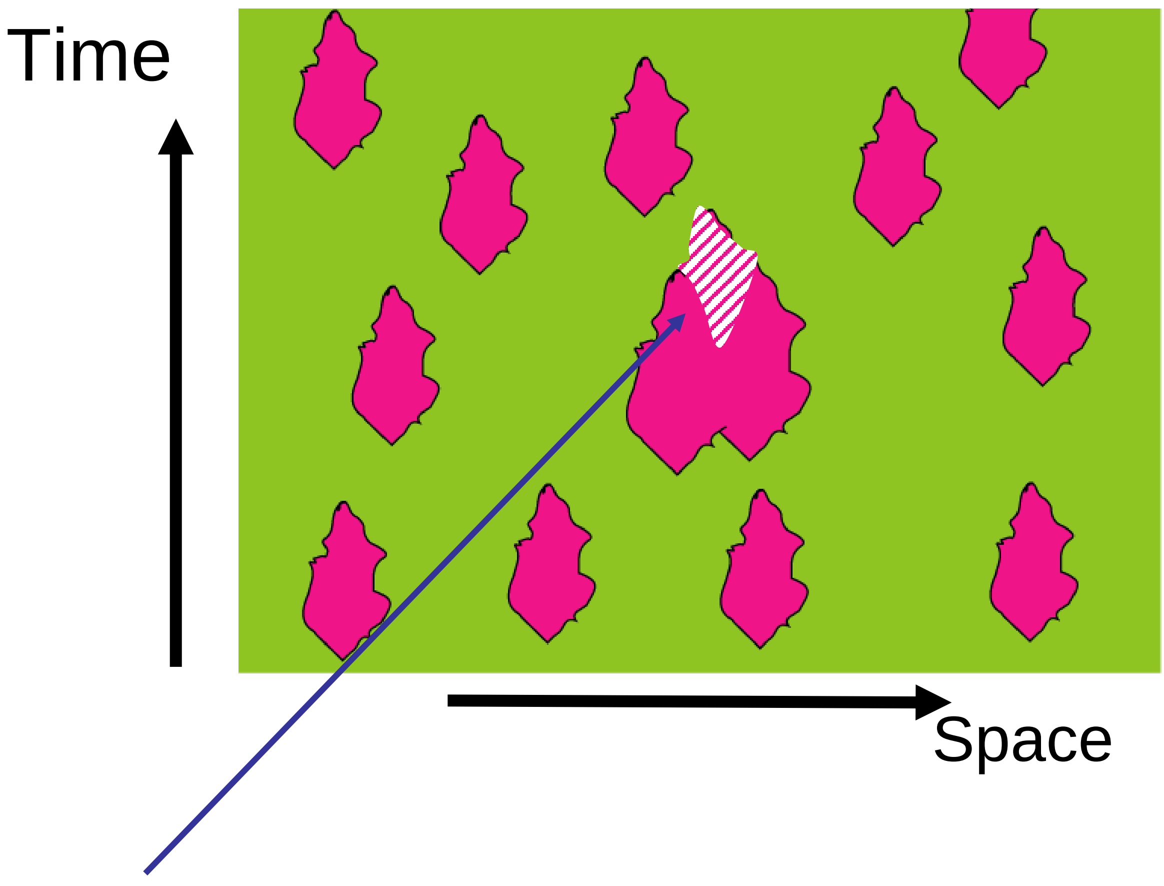
Genetic load independent bubbles



$$\text{fraction of mutants} \equiv q = \frac{U_d D}{2\mathrm{v}^2}, \quad \text{indep. of } K$$

O.H., D. R. Nelson (2008) ArXiv:0810.0053 [q-bio.PE]

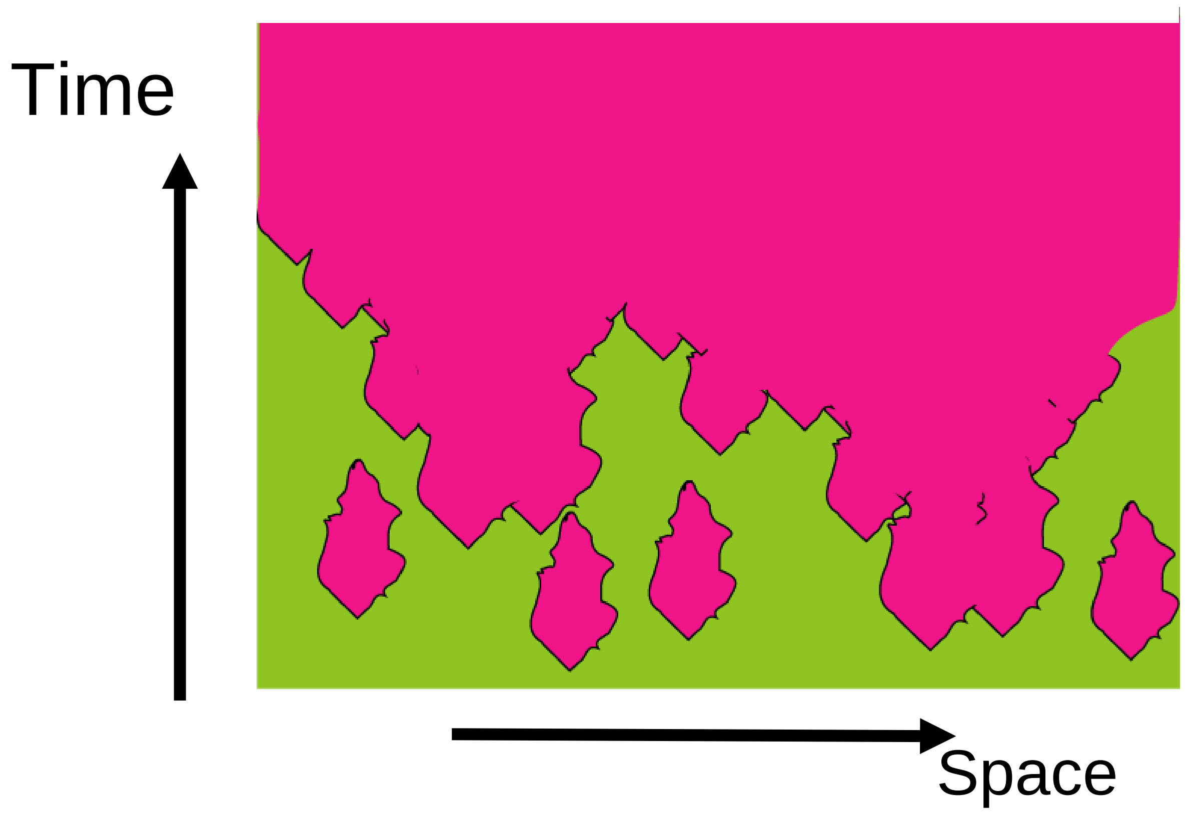
Genetic load, interacting bubbles



2 x Expected Area of a single bubble < Expected Area of a doublet

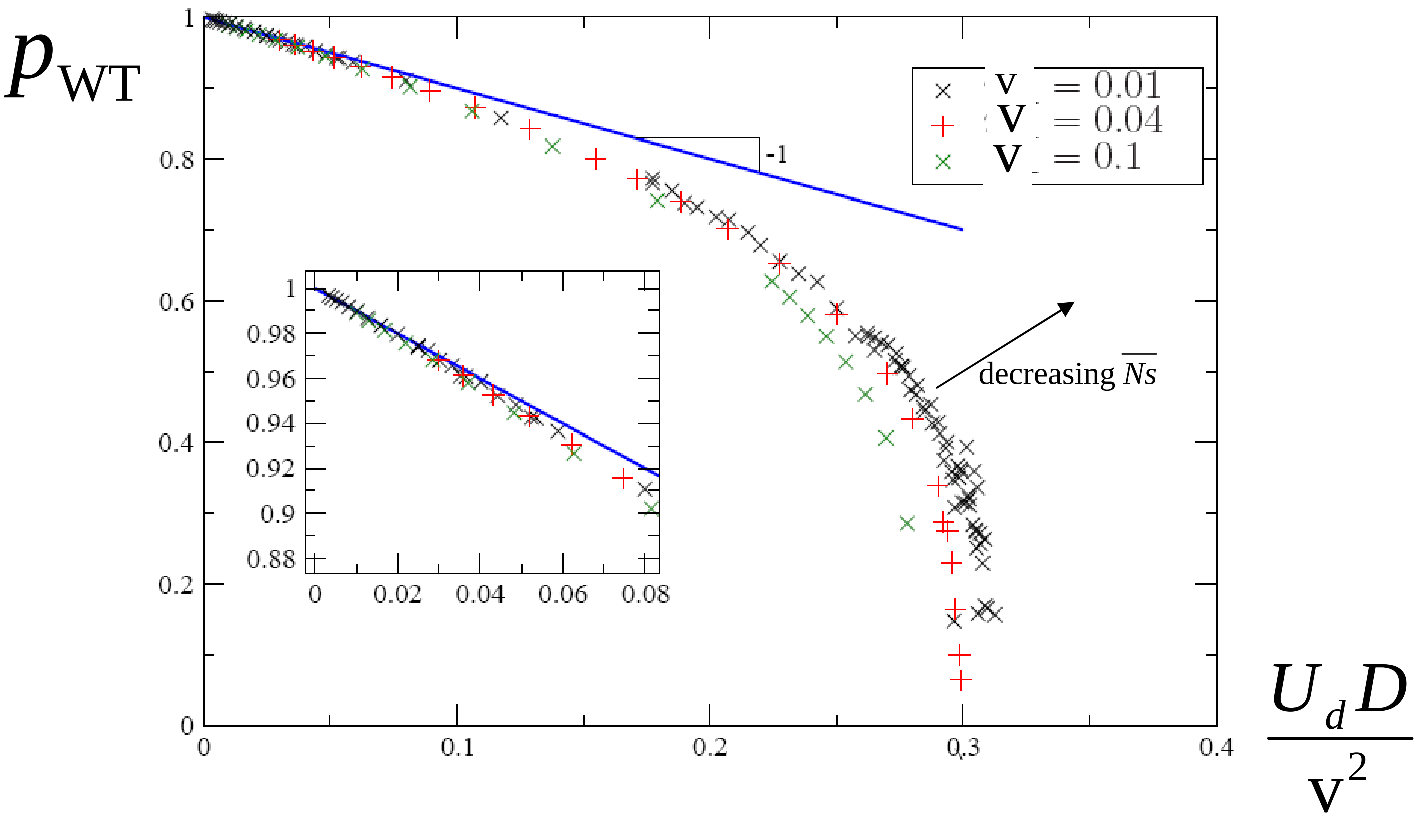
$$q = f\left(\frac{U_d D}{2v^2}\right)$$

Genetic load



Loss of wildtype for $U_d > U_{crit} \sim \frac{v^2}{D} \sim D(Ks)^2, \quad "Ns" < 1$

Genetic load is a function of one compound parameter



Universality class of

“directed percolation”

Summary

Compared to well-mixed populations, Hill-Robertson effects in spatial systems

- have qualitatively different impact
- are more common
- could possibly be tested with microbes

Thanks to …

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- Tom Shimizu, Howard Berg, Erin O'Shea, J. Krug
- Andrew Murray, Nilay Karahan
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For more information:

O. H., D. R. Nelson (2008) *Theoretical Population Biology* 73, 158-170
O. H., P. Hersen, S. Ramanathan, David R. Nelson (2007) *Proceedings of the National Academy of Sciences USA* 104, 19926-19930
O.H., D. R. Nelson (2008) ArXiv:0810.0053 [q-bio.PE]
L. Excoffier, N. Ray, Trends in Ecology & Evolution, 23(7):347–351, 7 2008.