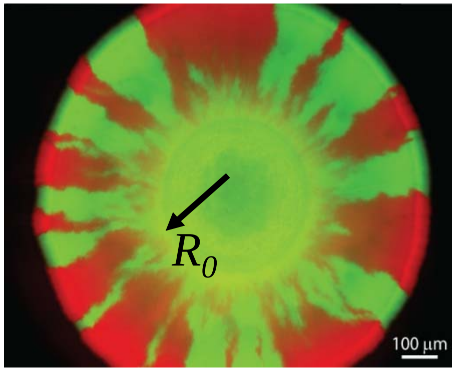
The Physics of Life: Spatial Population Genetics

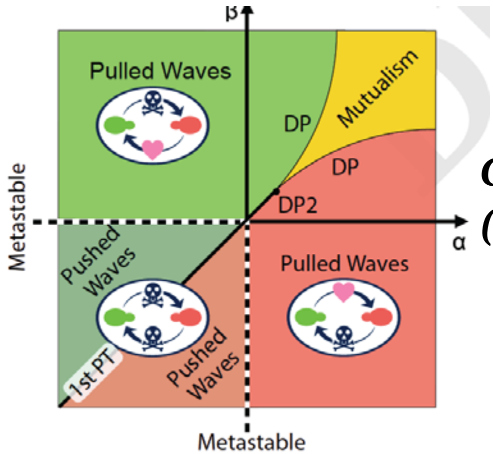
I. Introduction to spatial population genetics

II. Pushed genetic waves and antagonistic interactions

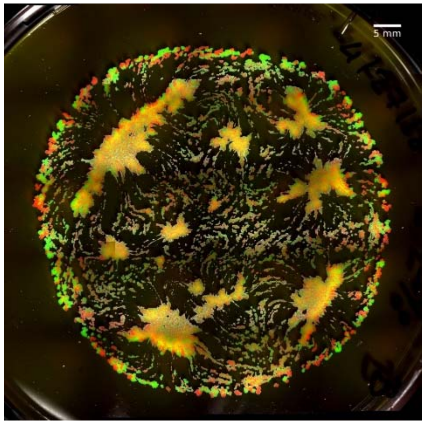
III. Microbial interactions and expansions on liquid substrates



P. Aeruginosa (J. Xavier et al.)

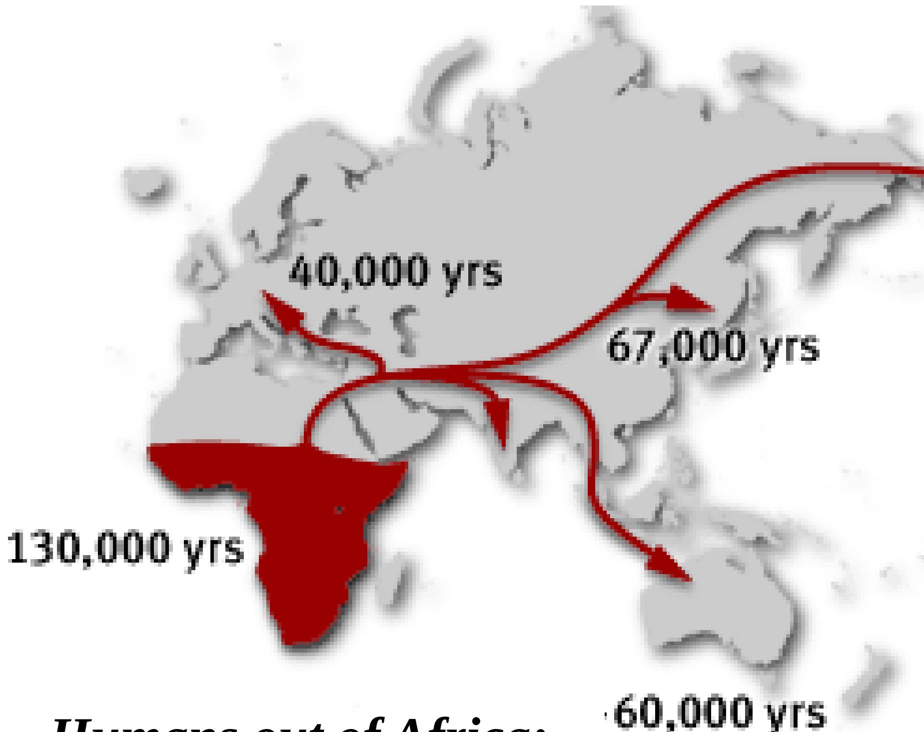


Game theory: (E. Frey et al.)



S. cerevisea (S. Atis et al.)

I. Introduction to spatial population genetics



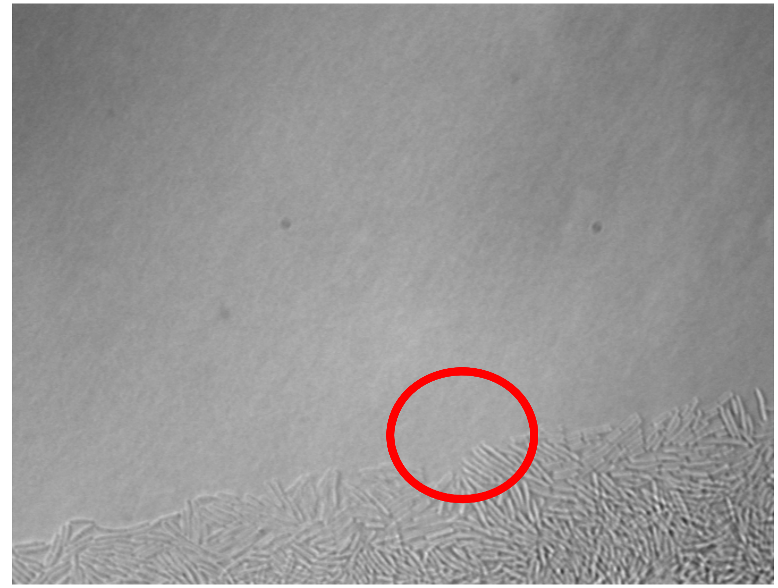
Humans out of Africa; in 500 generations...

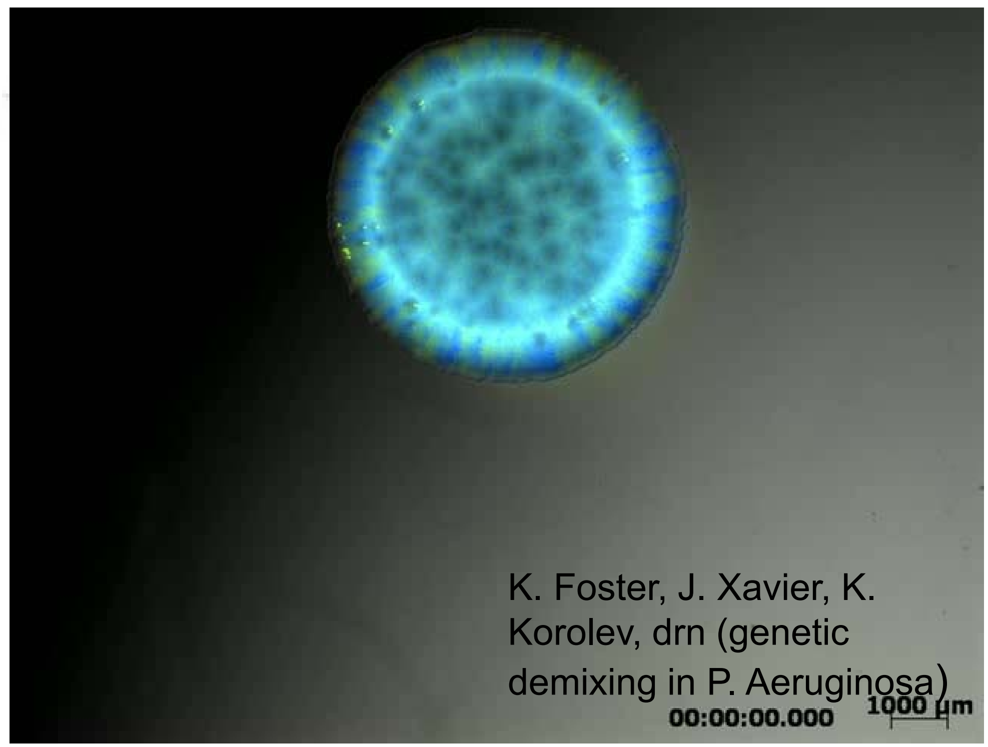
Large mammals expand over ~10^4 km

Bacteria (in a Petri dish) expand ~ 1 cm

*K. Korolev et al., Reviews of Modern Physics **82**, 1691 (2010)*

Oskar Hallatschek & drn, (E. coli)



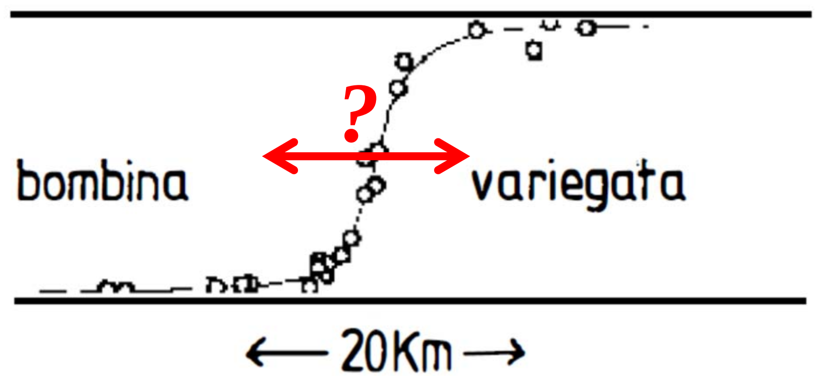


K. Foster, J. Xavier, K. Korolev, drn (genetic demixing in P. Aeruginosa)

II. Pushed genetic waves and antagonistic interactions: Hybrid zones

N. H. Barton & G. M. Hewitt Ann. Rev. Ecol. & Sys. **16**, 113 (1985)

- Hybrid zones are narrow regions in which genetically distinct populations meet, mate and produce hybrids. Hundreds of examples known. (e.g., the grasshopper *Podisma pedestris*, the butterfly *Heliconis.)* Hybrid zones can be a few hundred meters thick and hundreds of kilometers long

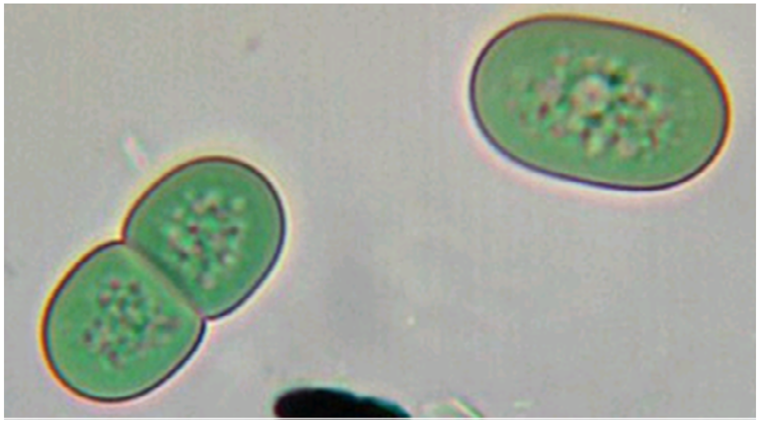


Inferred profile from electrophoretic variations across the hybrid zone of the toads *Bombina bombina* and *Bombina variegata* near Cracow, Poland

- *Which way the interface moves depends on more than just the selective advantage – for example, recombination near the interface can break up favorable clusters of genes.*
- *In some cases, boundaries can exhibit a kind of surface tension, as well as a pressure to advance in a particular direction. This may promote sympatric speciation*

III. Microbial interactions and expansions on liquid substrates

… life probably evolved first in a *liquid* environment



Cyanobacterium *Synechococcus*

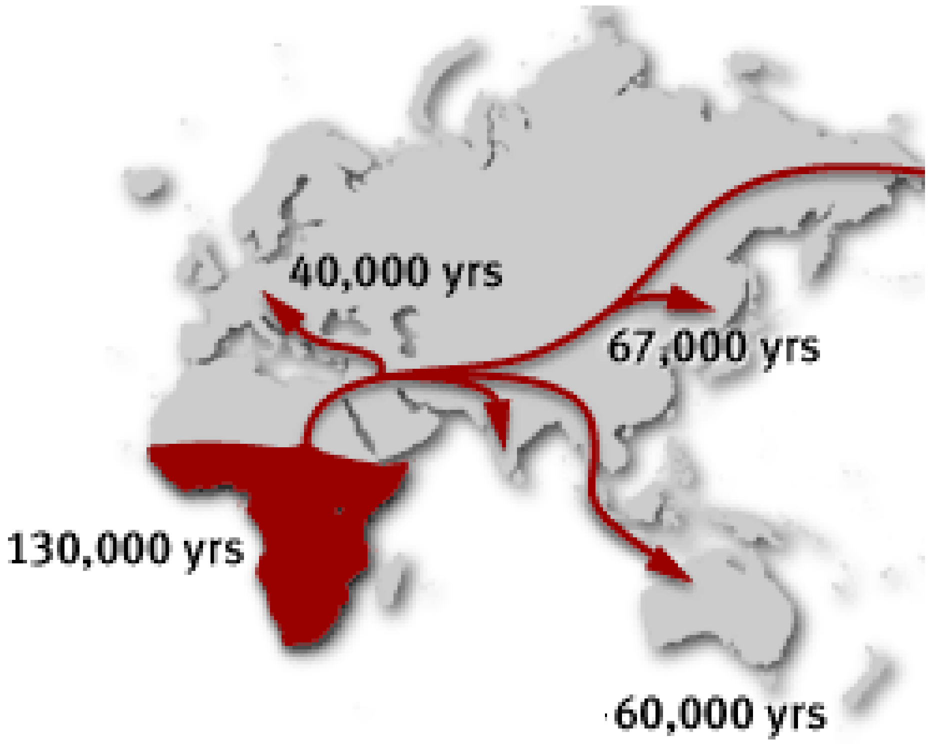
www.dr-ralf-wagner.de/Blaualgen-englisch.htm

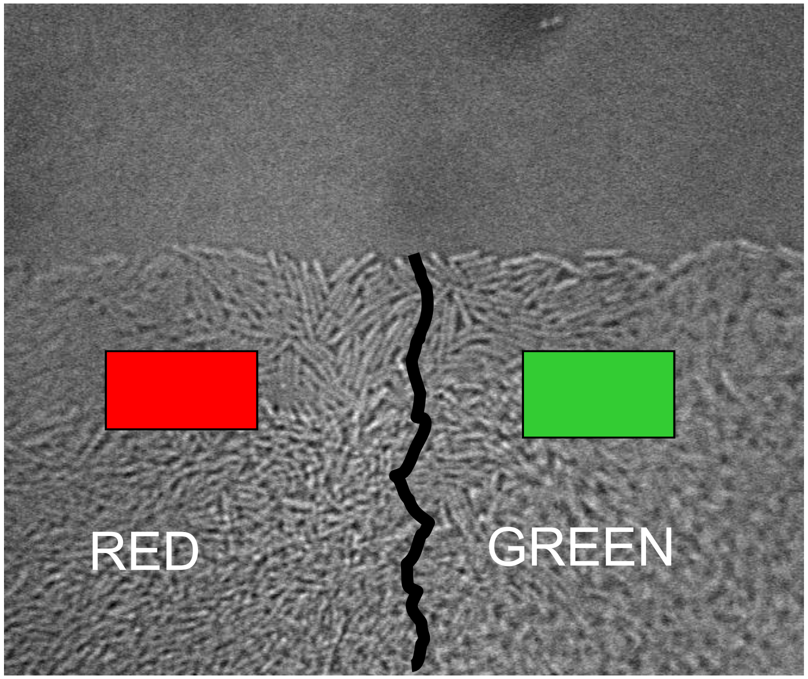
- ***~2-3 billion years ago, water covered most of the earth***
- ***Fossilized, oxygen-producing cyanobacteria have been dated at ~2 billion years ago.***
- ***Oxygenic cyanobacteria transformed the atmosphere via photosynthesis***
- ***Spatial growth and evolutionary competition took place in liquid environments at both high low Reynolds numbers***
- ***These photosynthetic organisms may control their height to resist down welling currents and stay close to the ocean surface.***

Bloom of cyanobacteria in Lake Atitlán, Guatemala

NASA Earth observatory

Range Expansions with Competition or Cooperation





In 500 generations….

Large mammals expand over ~10^4 km

Bacteria (in a Petri dish) expand ~ 1 cm

Red and Green Strains….

1. *Could be neutral….*
2. *Could have different doubling times*
3. *One or both could secrete toxins that impede the other…*
4. *One or both could secrete amino acids useful to the other: mutualism*

Gene Surfing and Survival of the Luckiest

Mutuations and competition in a spreading population

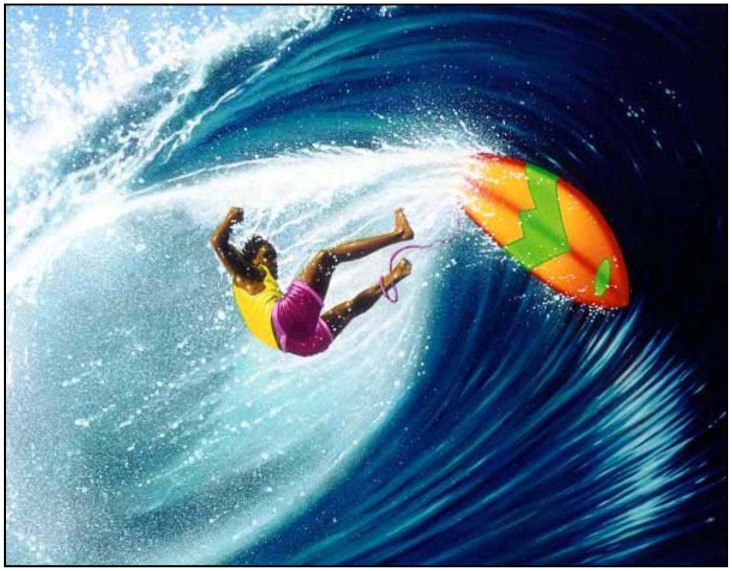
FAS Center for Systems Biology

Lots of help in the lab from Pascal Hersen and Sharad Ramanathan

Oskar Hallatschek

Kirill Korolev

vs.



Gene Surfing and Survival of the Luckiest

Mutations and competition in a spreading population

Surfing on the Einsbach,
Englischer Garten, Munich...

Successful....

Unsuccessful….

Fisher Waves and Population Dynamics

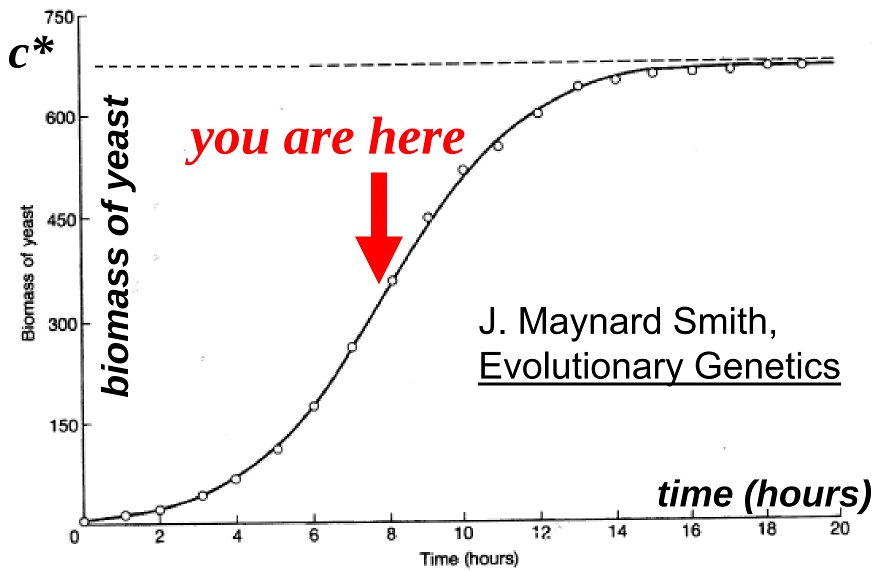
$c(t) =$ population of species at time t in region Ω

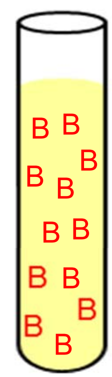
$$\frac{dc(t)}{dt} = \text{births - deaths + saturation + migration}$$

1798 T.R. Matthus $\quad \frac{dc(t)}{dt} = ac(t), \; a > 0$

1836 P.F. Verhulst $\quad \frac{dc(t)}{dt} = ac(t) - bc^2(t) \qquad c(t) = \frac{c(0)e^{at}}{1 + \left(c(0)b/a\right)(e^{at} - 1)}$

stable population size: $c^* = a/b$





1937 R.A. Fisher, Kolmogorov et al.

$c = c(\vec{r}, t) \qquad \frac{\partial c(\vec{r},t)}{\partial t} = D\nabla^2 c(\vec{r},t) + ac(\vec{r},t) - bc^2(\vec{r},t)$

a

Wave Solutions to the Fisher-Kolmogorov et al. Equation

in one-dimension...

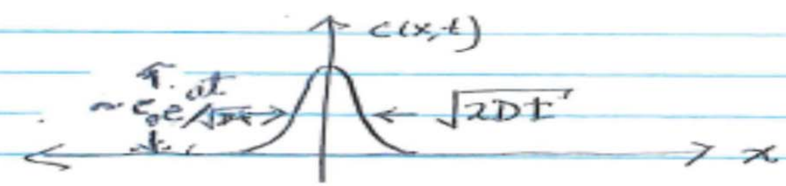
$$\frac{\partial c(x,t)}{\partial t} = D\frac{\partial^2 c(x,t)}{\partial x^2} + a\,c(x,t) - b\,c^2(x,t) \qquad (\star)$$

* If $c(x,0)$ is small ($c(x,0) << c^* = a/b$), then early time behavior is given by the solution of the linear equation $\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + ac$

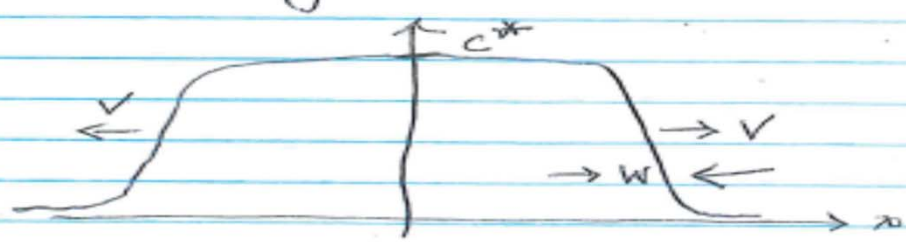
Namely,

$$c(x,t) = c_0 e^{at} \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$

$\Rightarrow$ $c(x,t)$ spreads out diffusively, but grows up exponentially as well...
$\int c(x,t)\,dx = c_0 e^{at}$



* but eventually $c(x,t) \lesssim c^*$ & new behavior arises

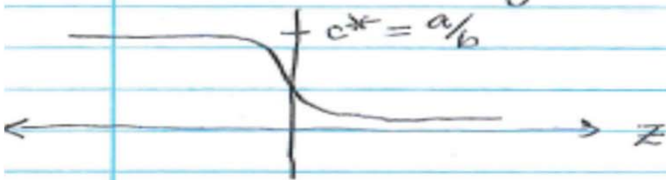


V = ?
W = ?

b

* Dynamical Systems approach ...

Look for solutions of ⊛ that interpolate from $c = c^* = \frac{a}{b}$ to $c = 0$ in the form of a wave moving from left to right ...



$$c(x,t) = f(x - vt) = f(z)$$
$$\lim_{z \to -\infty} f(z) = a/b$$
$$\lim_{z \to \infty} f(z) = 0$$

$$\Rightarrow \; -v f'(z) = D f''(z) + a f(z) - b f^2(z) \quad ⊛$$

* Regard z as a time-like variable & define a "momentum" variable $g(z) = \frac{df}{dz}$

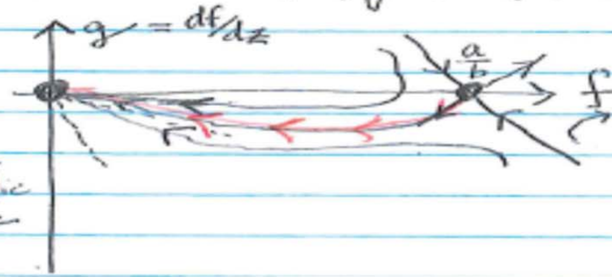
Then ⊛ can be written as two ordinary differential equations

$$\frac{dg(z)}{dz} = -\frac{v}{D} g(z) - \frac{a}{D} f(z) + \frac{b}{D} f^2(z)$$
$$\frac{df(z)}{dz} = g(z)$$

Fixed points are $(f^*, g^*) = (0, 0)$ & $(f^*, g^*) = (\frac{a}{b}, 0)$

Phase Portrait

* The solution we want is clearly the trajectory connecting the hyperbolic fixed pt at $(0, a/b)$ to the origin!



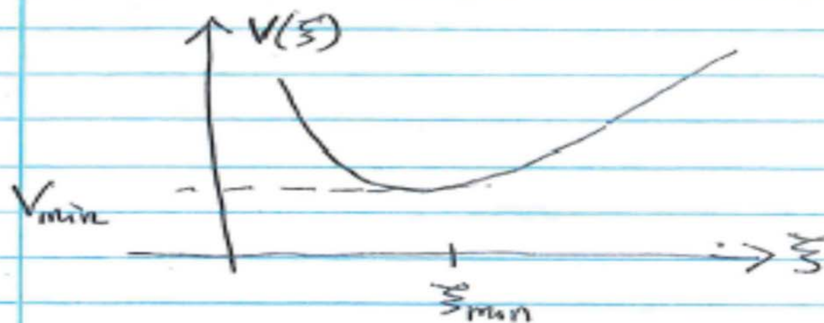
c

Velocity selection problem

However a solution seems to exist for a range of v's!

* Can get a bound on v by looking at the (right) foot of the wave & trying to solve the linear equation with $c(x,t) \approx c_0 e^{(x-vt)/\xi}$

$$\Rightarrow \frac{v}{\xi} = \frac{D}{\xi^2} + a \Rightarrow \boxed{v = \frac{D}{\xi} + a\xi}$$ "dispersion relation"



$$\xi_{min} = \sqrt{\frac{D}{a}}$$

$$v_{min} = 2\sqrt{Da}$$

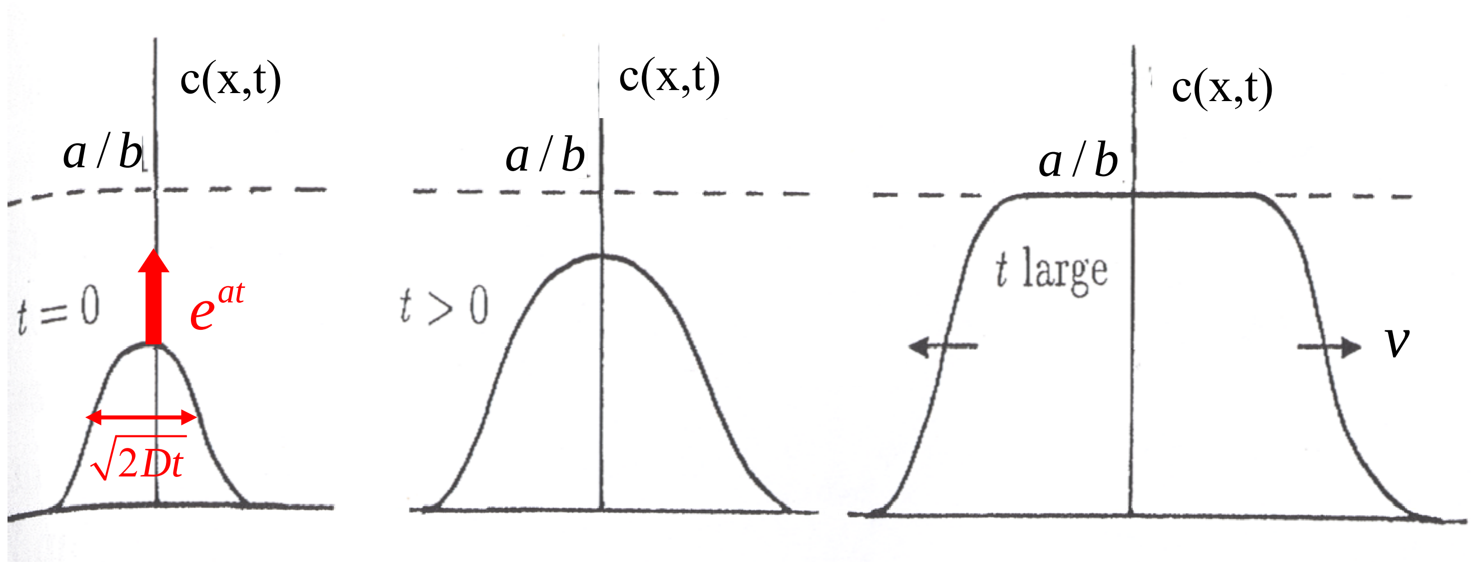
* Kolmogorov showed that the asymptotic velocities (moving right & left) for any initial condition with finite support is in fact $v = v_{min} = 2\sqrt{Da}$ with width $w = \xi_{min} = \sqrt{\frac{D}{a}}$

* More generally, velocity depends on the way $f(z)$ behaves as $z \to \pm\infty$
* Note that two exponential lengths appear for $v > v_{min}$!

Population & Genetic Waves In One Dimension

(R. A. Fisher, Kolmogorov-Petrovsky-Piscounov, 1937)

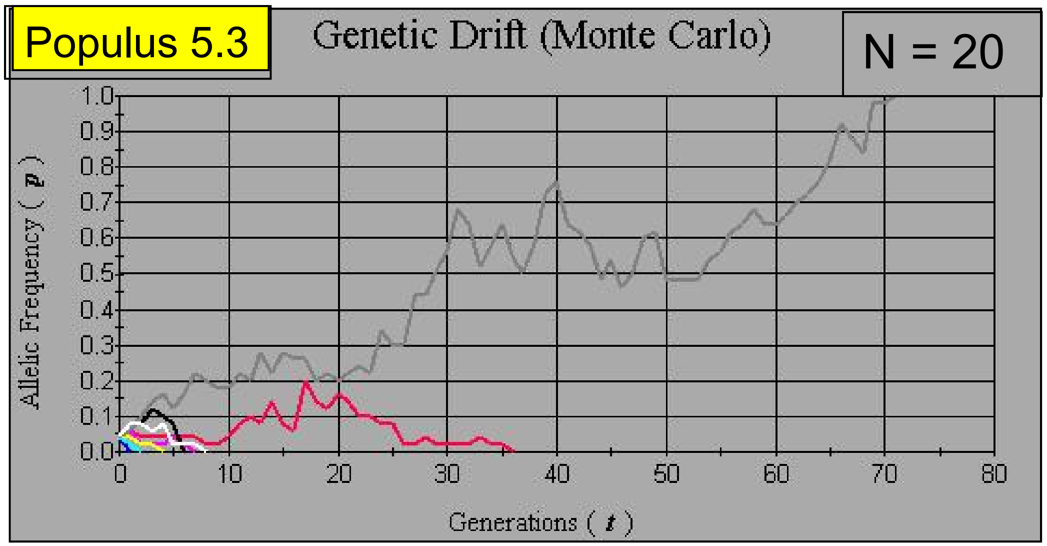
$$\frac{\partial}{\partial t}c(x,t) = D\frac{\partial^2}{\partial x^2}c(x,t) + ac(x,t)[1 - bc(x,t)/a]; \quad let\ c(x,t) = f(x - vt)$$



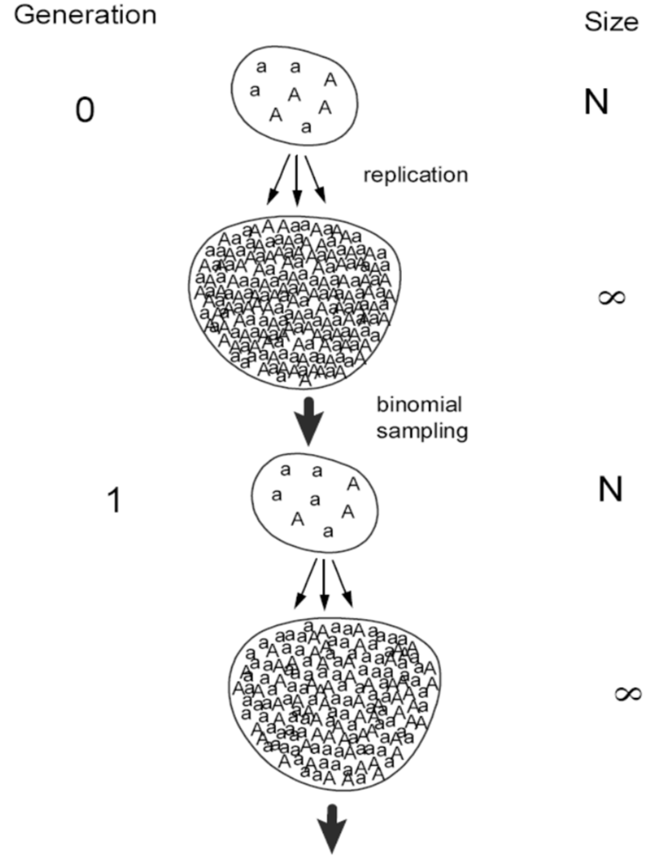
Schematic time development of a wavefront solution of Fisher's equation on the infinite line. (J.D. Murray, Mathematical Biology)

$$Interface\ velocity = 2\sqrt{Da} \qquad Interface\ width = \sqrt{D/a}$$

Genetic drift for a neutral mutation, (M. Kimura)



u(p,t)= probability allele A has frequency p at time t.



Finite populations go to fixation for long times(using, e.g., Fisher-Wright population sampling)

$$\frac{\partial u(p,t)}{\partial t} = \frac{\partial^2 [D_G u(p,t)]}{\partial p^2}$$

$$D_G(p) = p(1-p)/(2N)$$

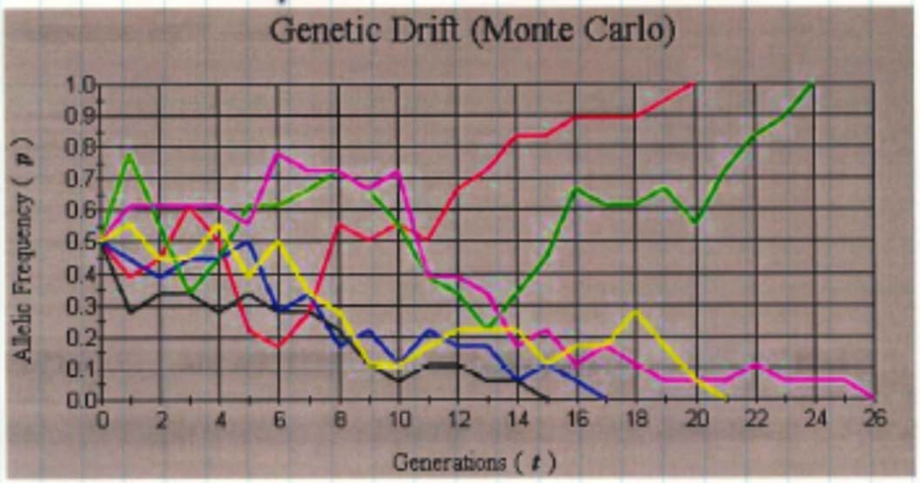
$$\frac{\partial p(t)}{\partial t} = \sqrt{p(t)(1-p(t))/N}\ \Gamma(t)$$

$$<\Gamma(t)\Gamma(t')> = \delta(t-t')\ \text{(Ito calculus)}$$

DIPLOID

Population Size: $N = 10$

INTRO. TO POPULATION GENETICS THEORY
J. F. Crow & M. Kimura



Allele frequencies ***diffuse*** *due to genetic drift ….*

M. Kimura, Genetics 47, 713 (1962)

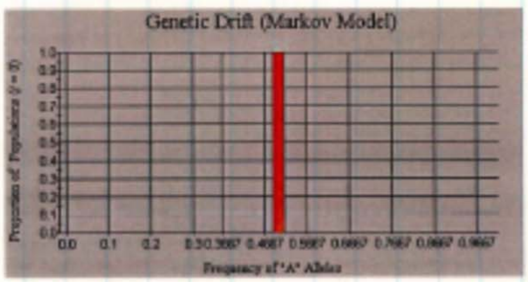
i.e. random walk dynamics of gene frequencies!

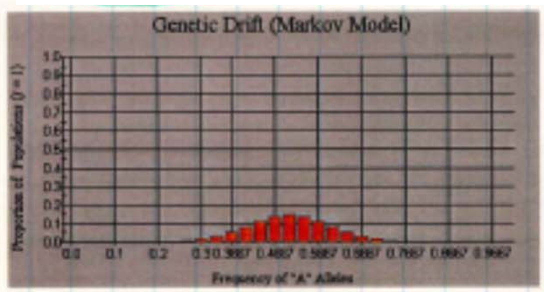
u(p,t)= probability allele A has frequency p at time t.

•Finite populations go to fixation for long times …

See Populus program…

$$\frac{\partial u(p,t)}{\partial t} = \frac{\partial^2}{\partial p^2}\left[\frac{p(1-p)}{4N}u(p,t)\right]$$





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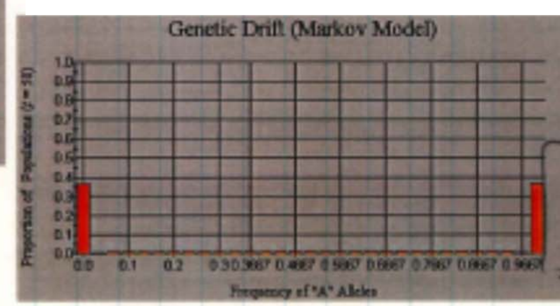


* All finite populations eventually fixed with homozygous population of all (a/a) or all (A/A)

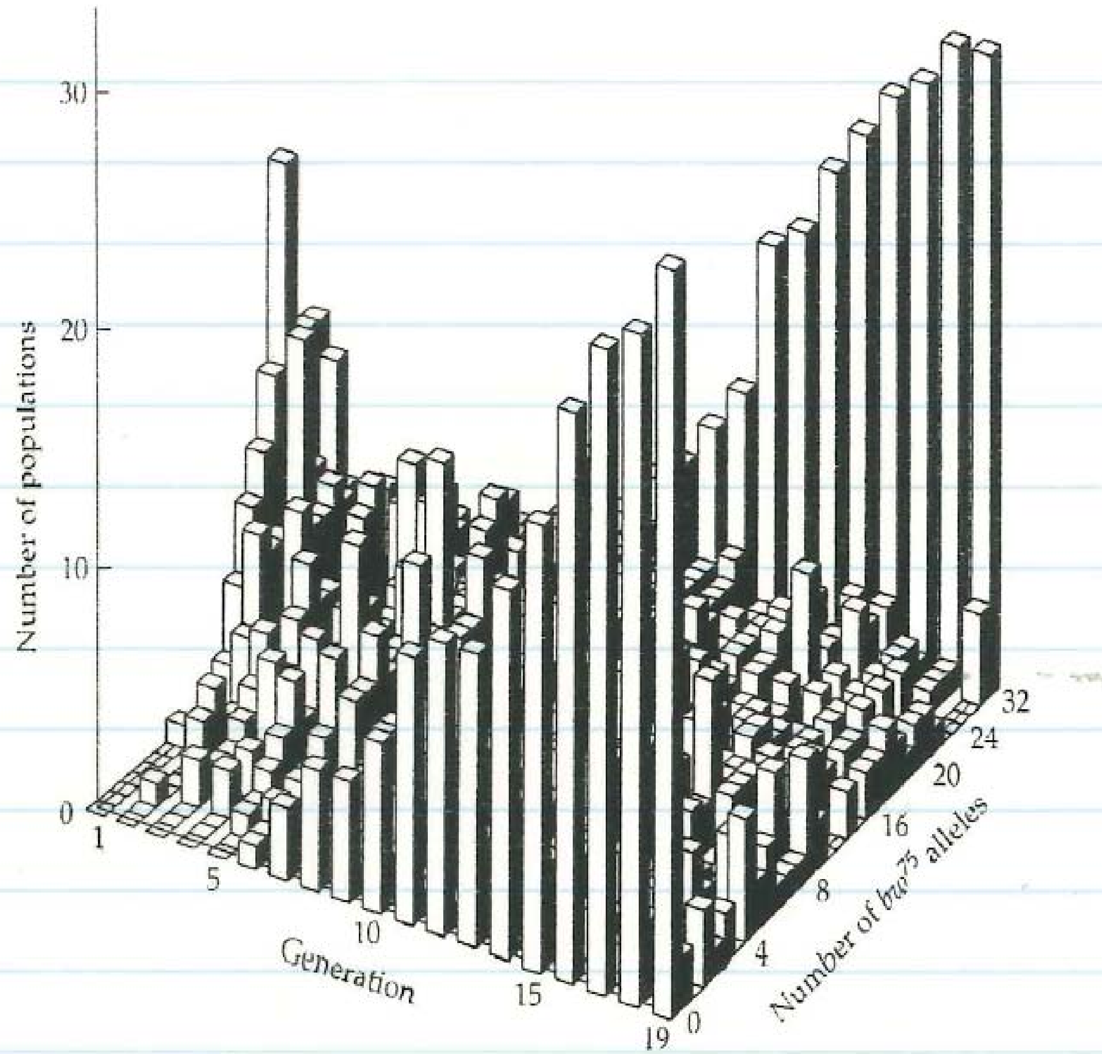


FIGURE 3.4 Random genetic drift in 107 actual populations of *Drosophila melanogaster*. Each of the initial 107 populations consisted of 16 bw^{75}/bw heterozygotes (N = 16; bw = brown eyes). From among the progeny in each generation, eight males and eight females were chosen at random to be the parents of the next generation. The horizontal axis of each curve gives the number of bw^{75} alleles in the population, and the vertical axis gives the corresponding number of populations. (Data from Buri 1956.)

Fixation of bw^{75} & bw alleles in 107 fruit fly populations with $N = 16$

PRINCIPLES OF POPULATION GENETICS FOURTH EDITION
Daniel L. Hartl
Andrew G. Clark

Numerical solution by Kimura (1955) of Kolmogorov forward equation...

$$\frac{\partial u(x,p,t)}{\partial t} = \frac{\partial^2}{\partial x^2}\left[\frac{x(1-x)}{4N}\, u(x,p,t)\right]$$

$$u(x,p,t=0) = \delta(x-p)$$

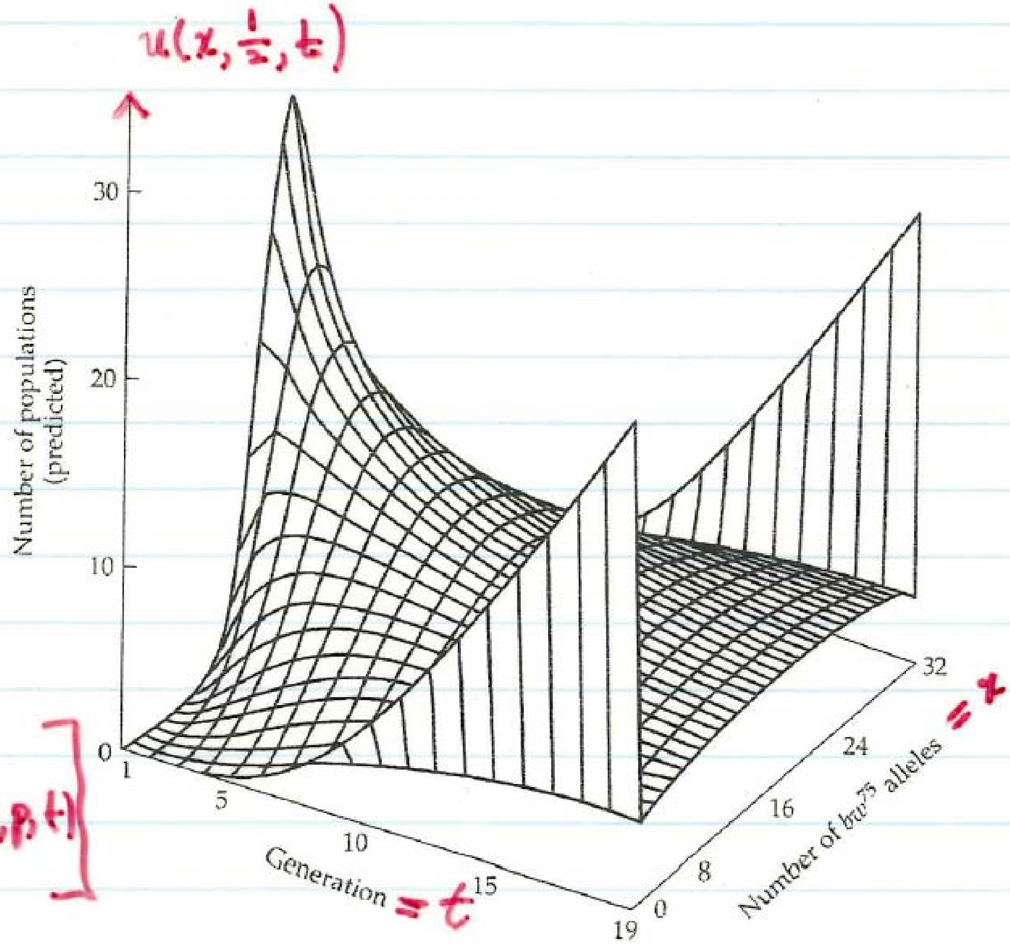
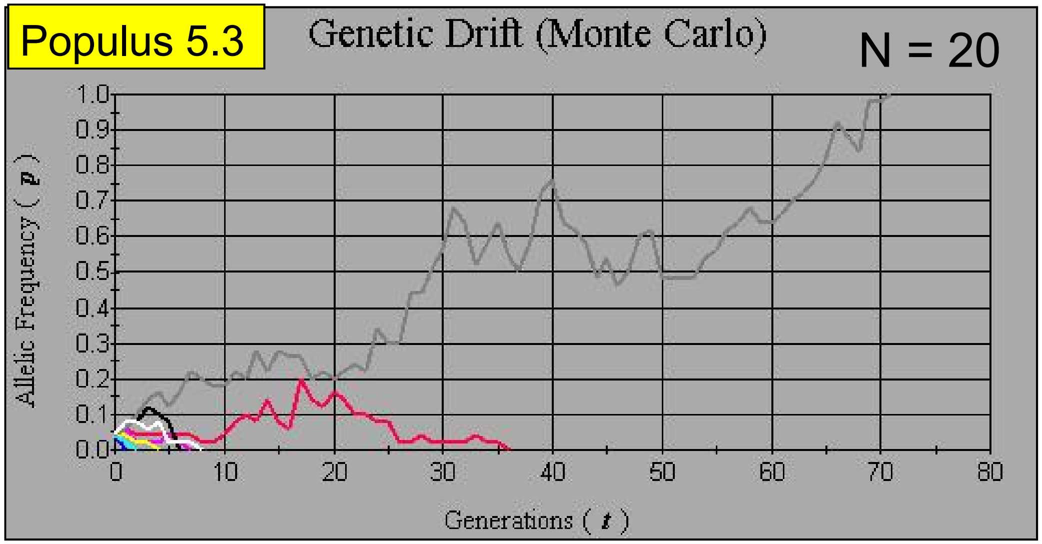
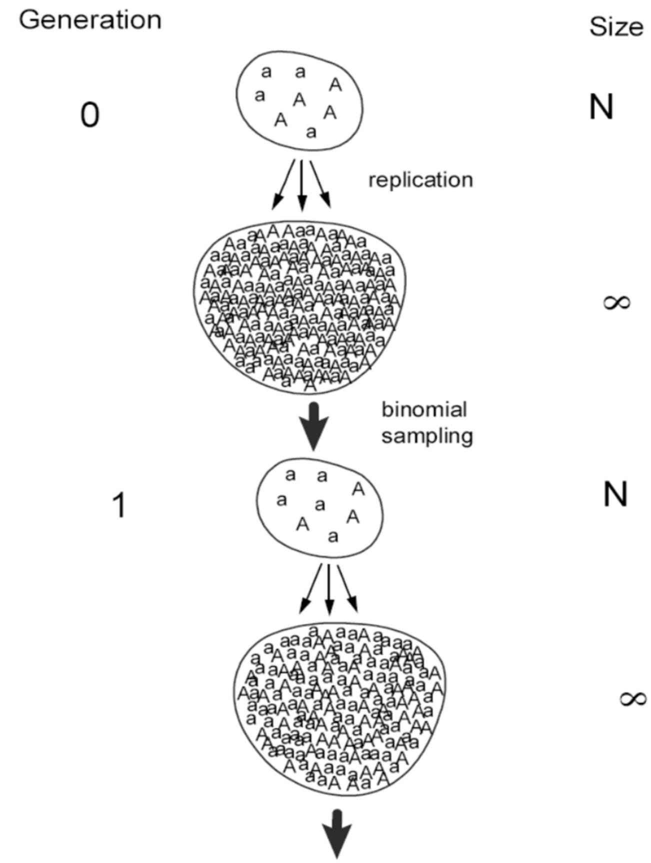


FIGURE 3.7 Kimura's (1955) solution to the diffusion equation for the particular case of $N = 16$. This is the three-dimensional view of Figure 3.6, and represents the diffusion approximation to the exact solution obtained from the Wright-Fisher model in Figure 3.5.

Genetic drift for a neutral mutation, (M. Kimura)





u(p,t)= probability allele A has frequency p at time t.

Finite populations go to fixation for long times(using, e.g., Fisher-Wright population sampling)

$$\frac{\partial u(p,t)}{\partial t} = \frac{\partial^2 [D_G u(p,t)]}{\partial p^2}$$

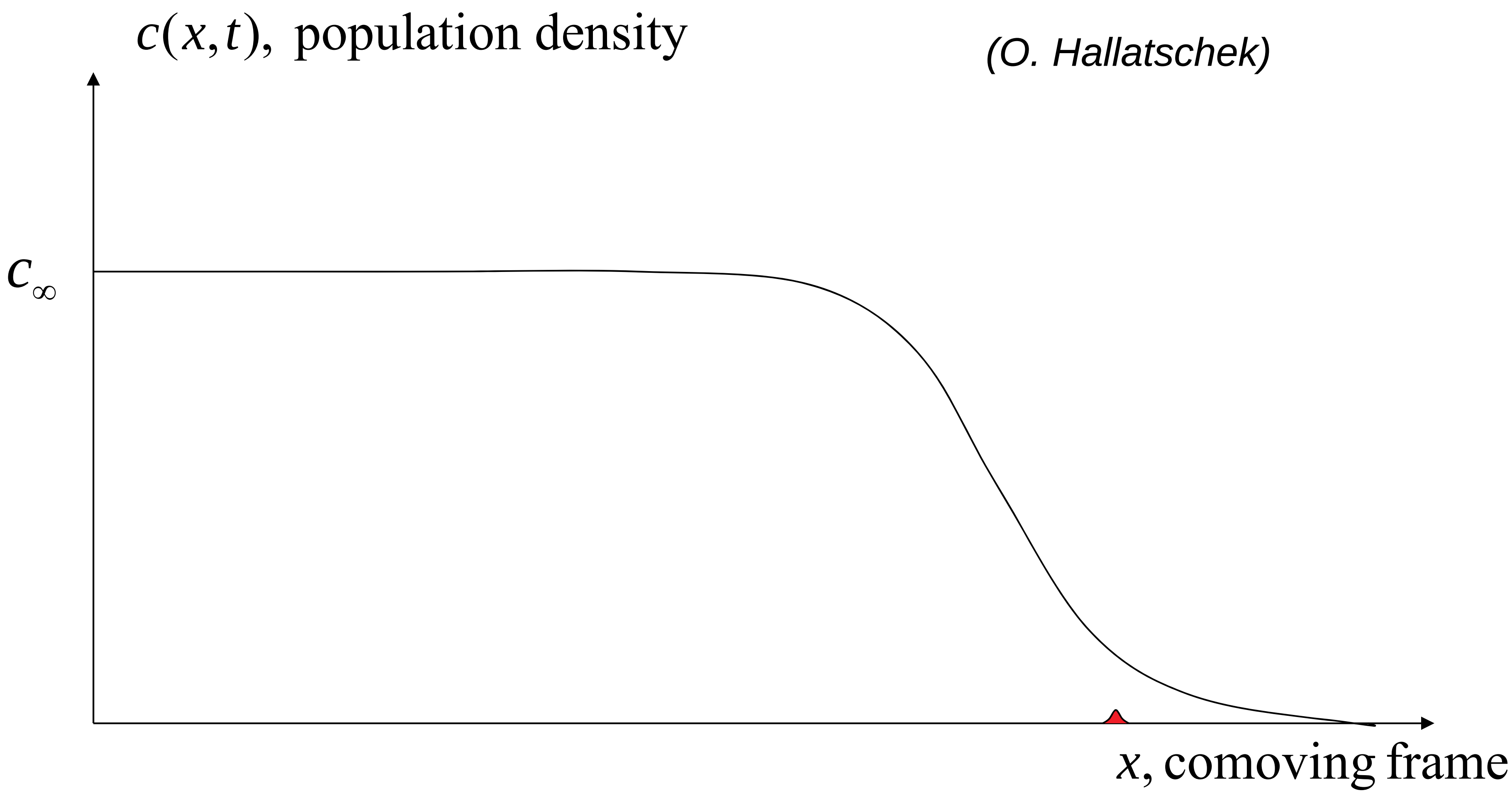
$$D_G(p) = p(1-p)/(4N)$$

Finite populations go to fixation for long times

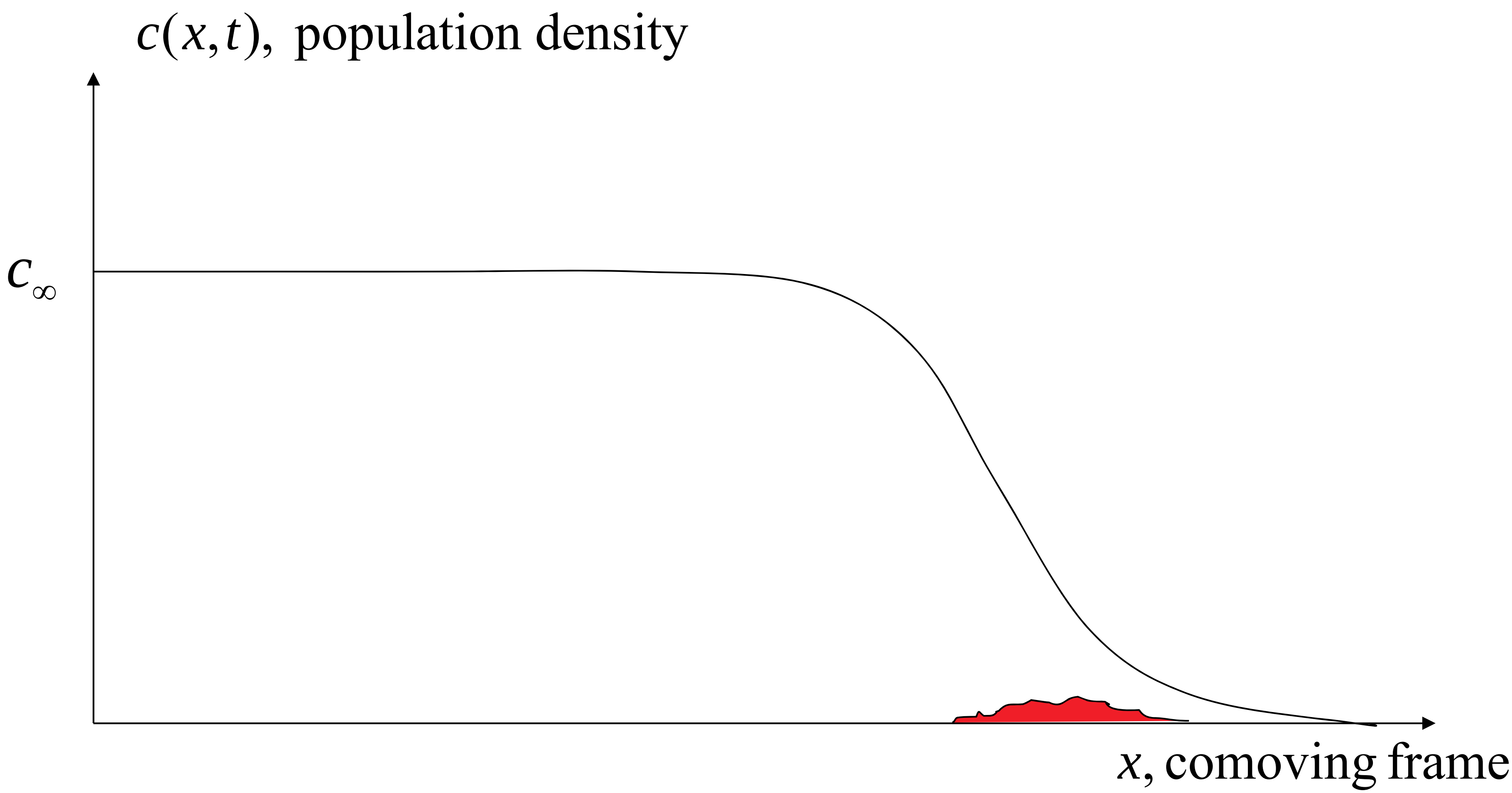
Probability of fixation of a single neutral mutation in a population of size N is just 1/N

But N is small in the vicinity of an expanding population front!

Successful Surfing (1d)



Successful Surfing (1d)



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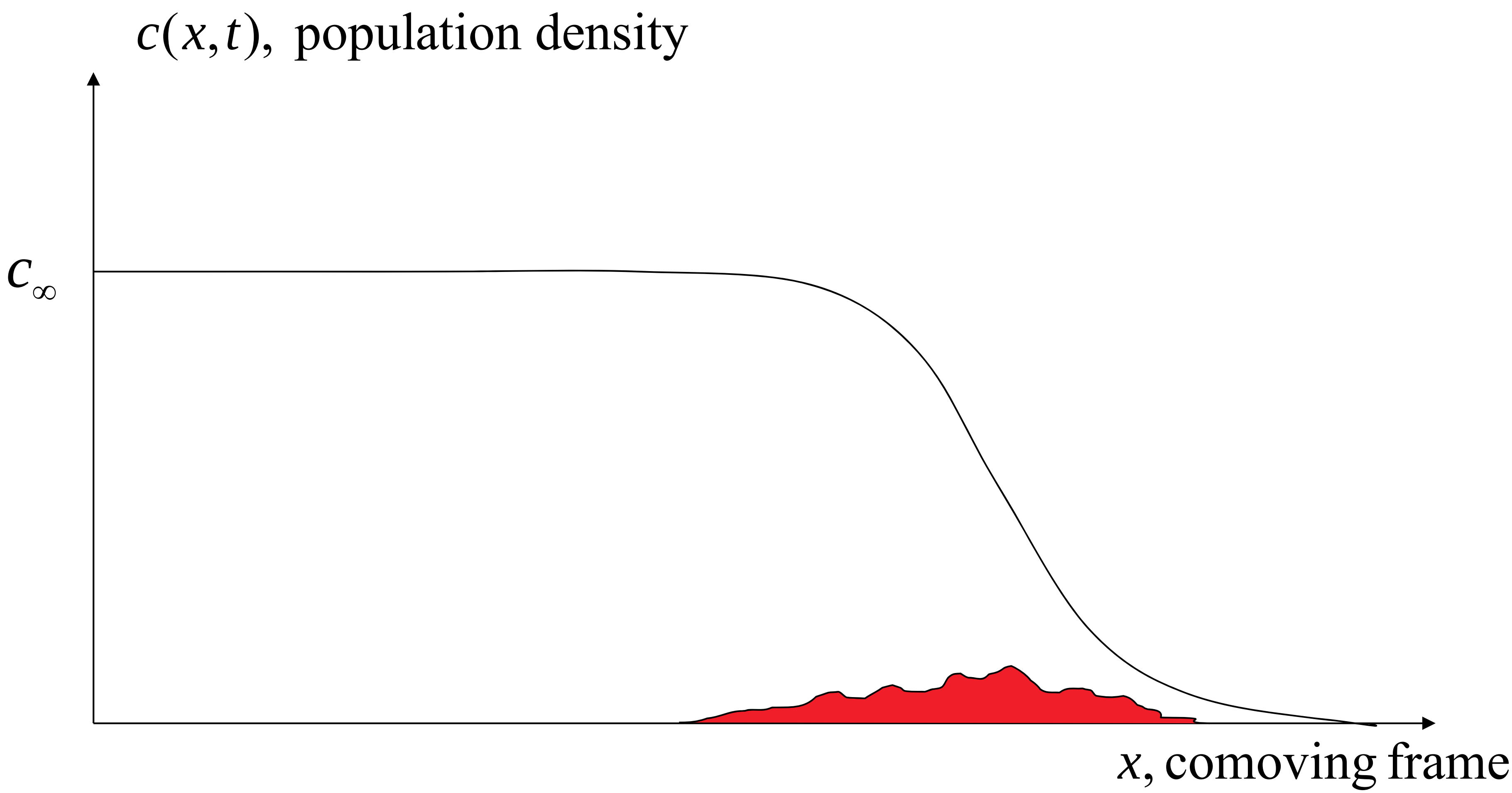
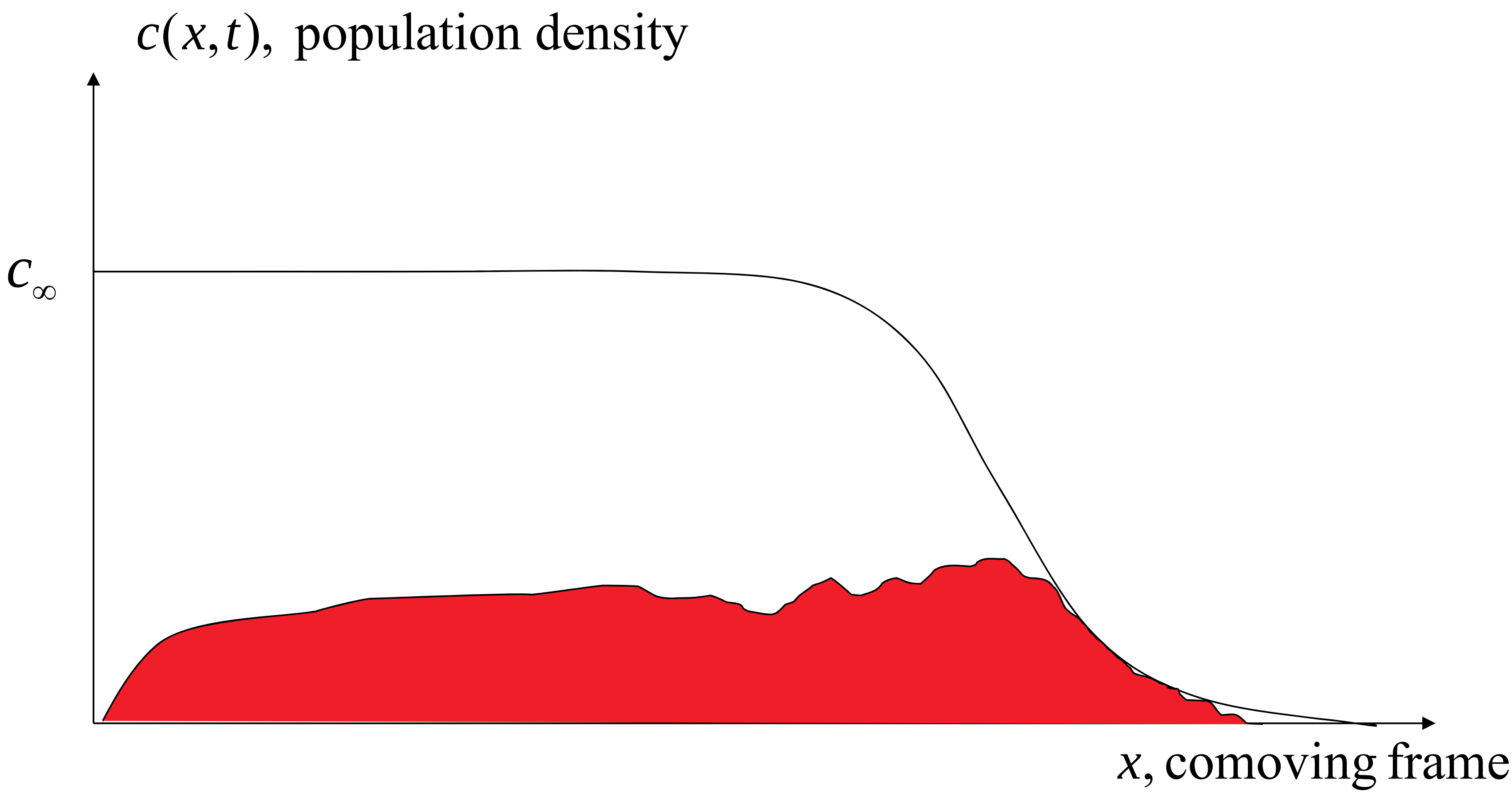
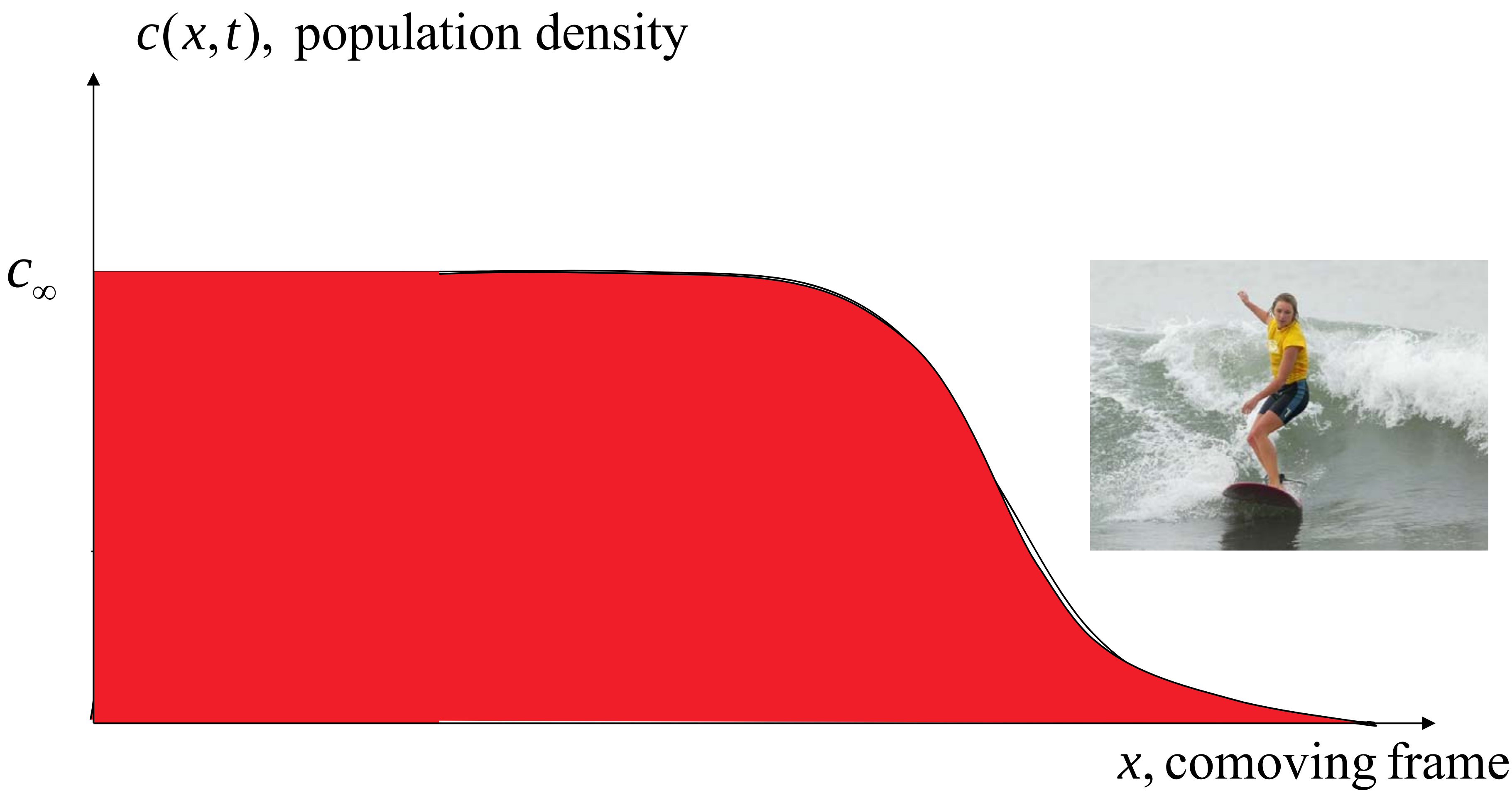


Successful Surfing (1d)

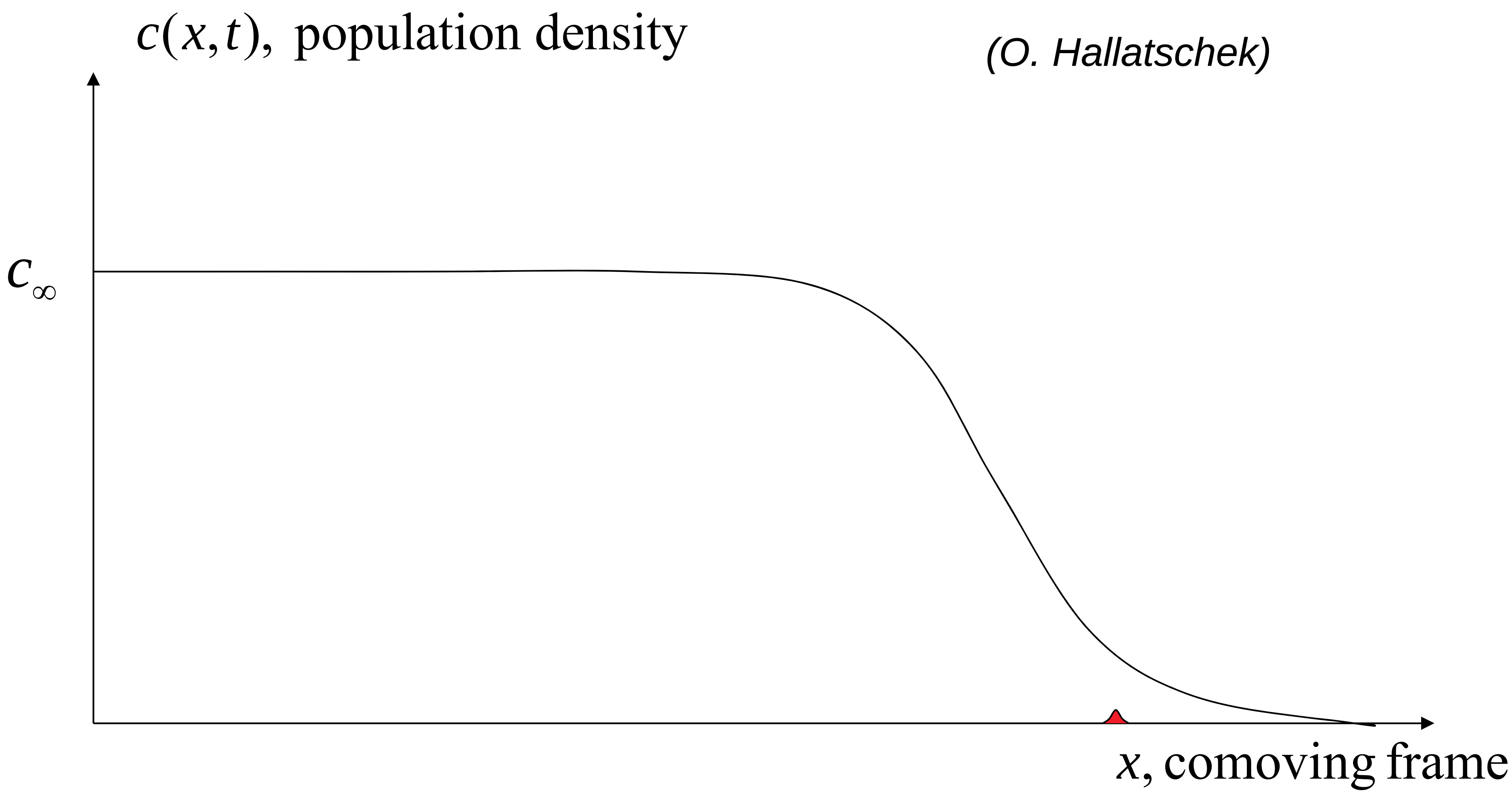


Successful Surfing (1d)

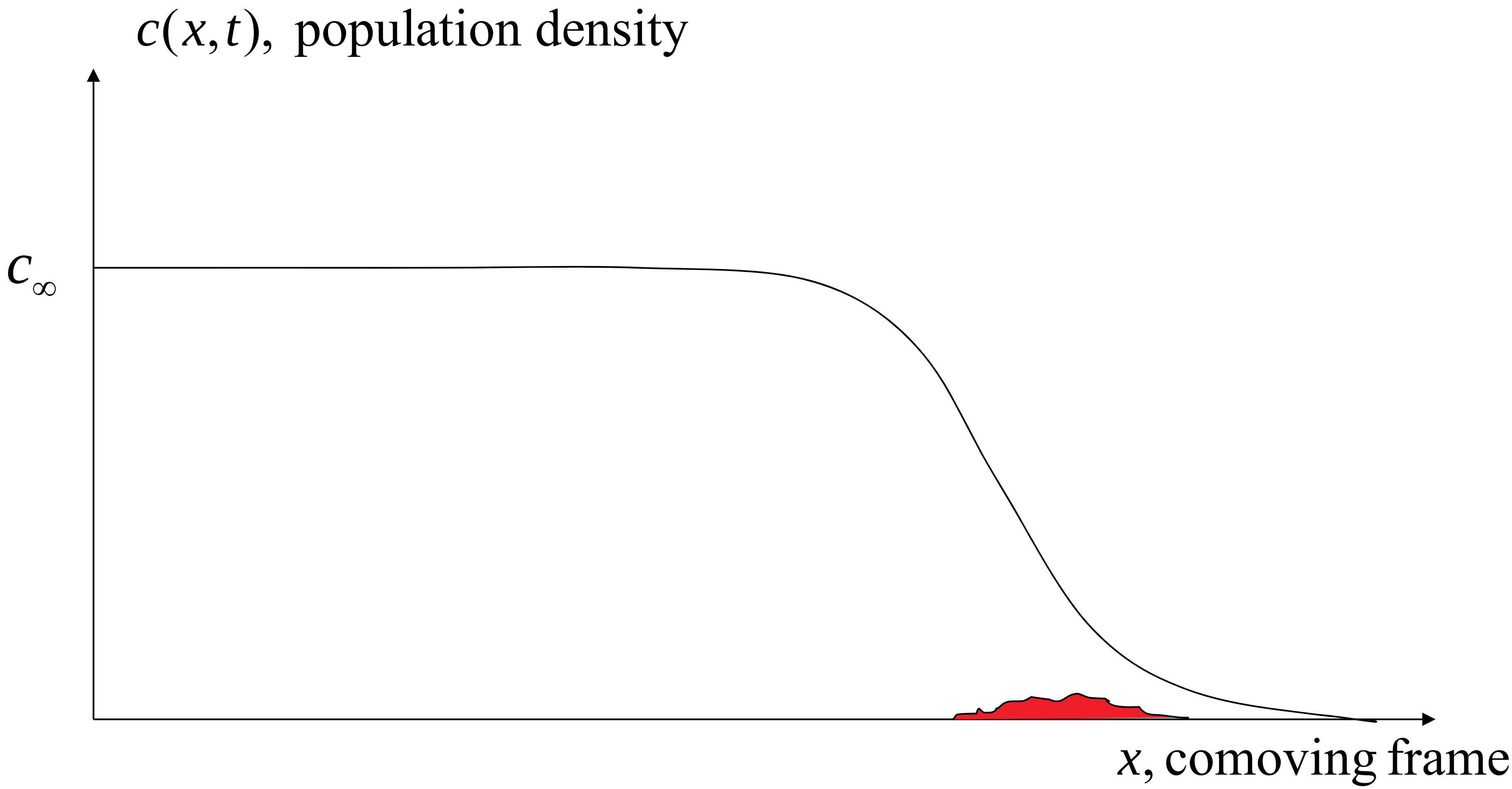


Often however …

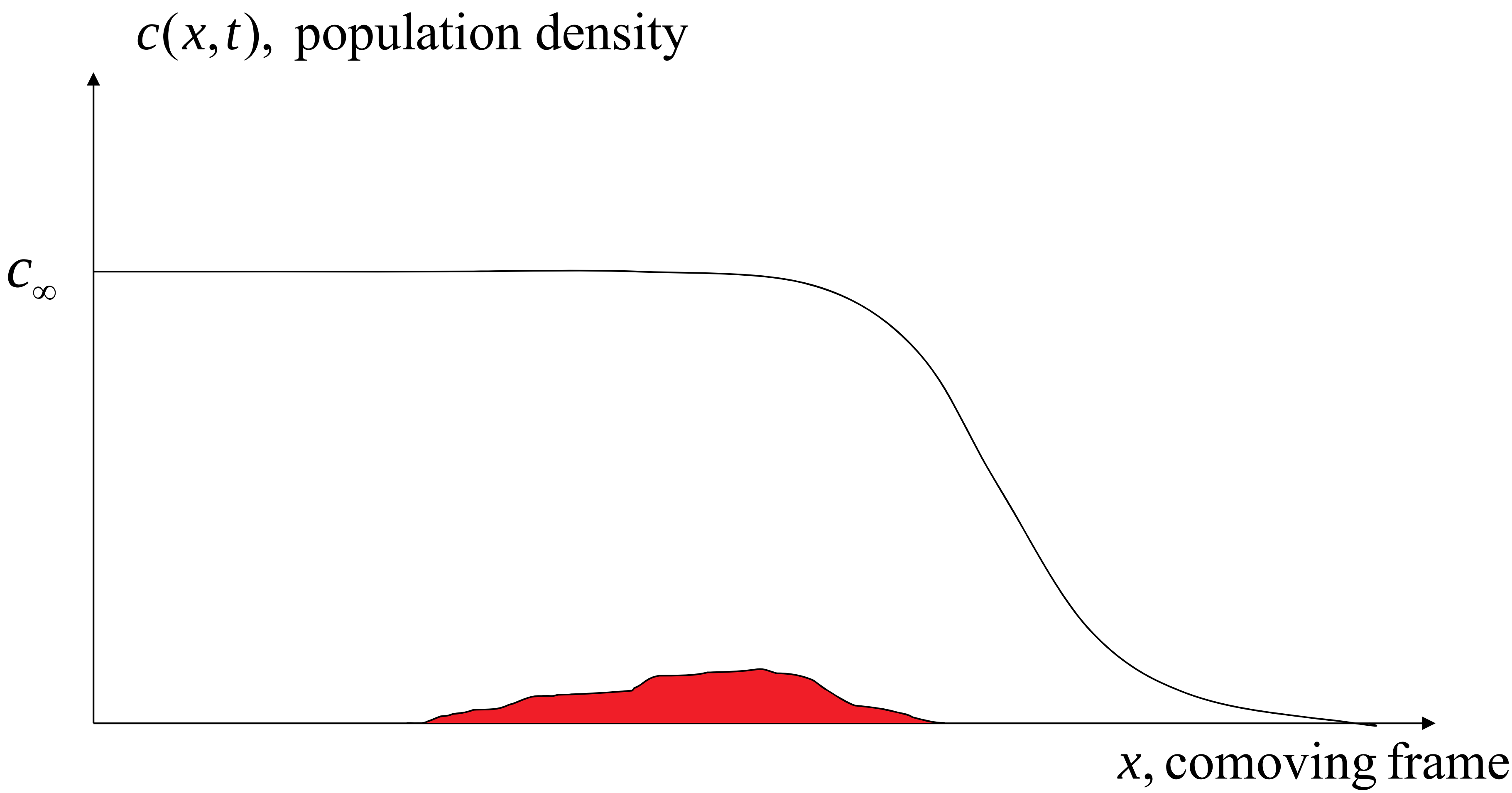
(O. Hallatschek)



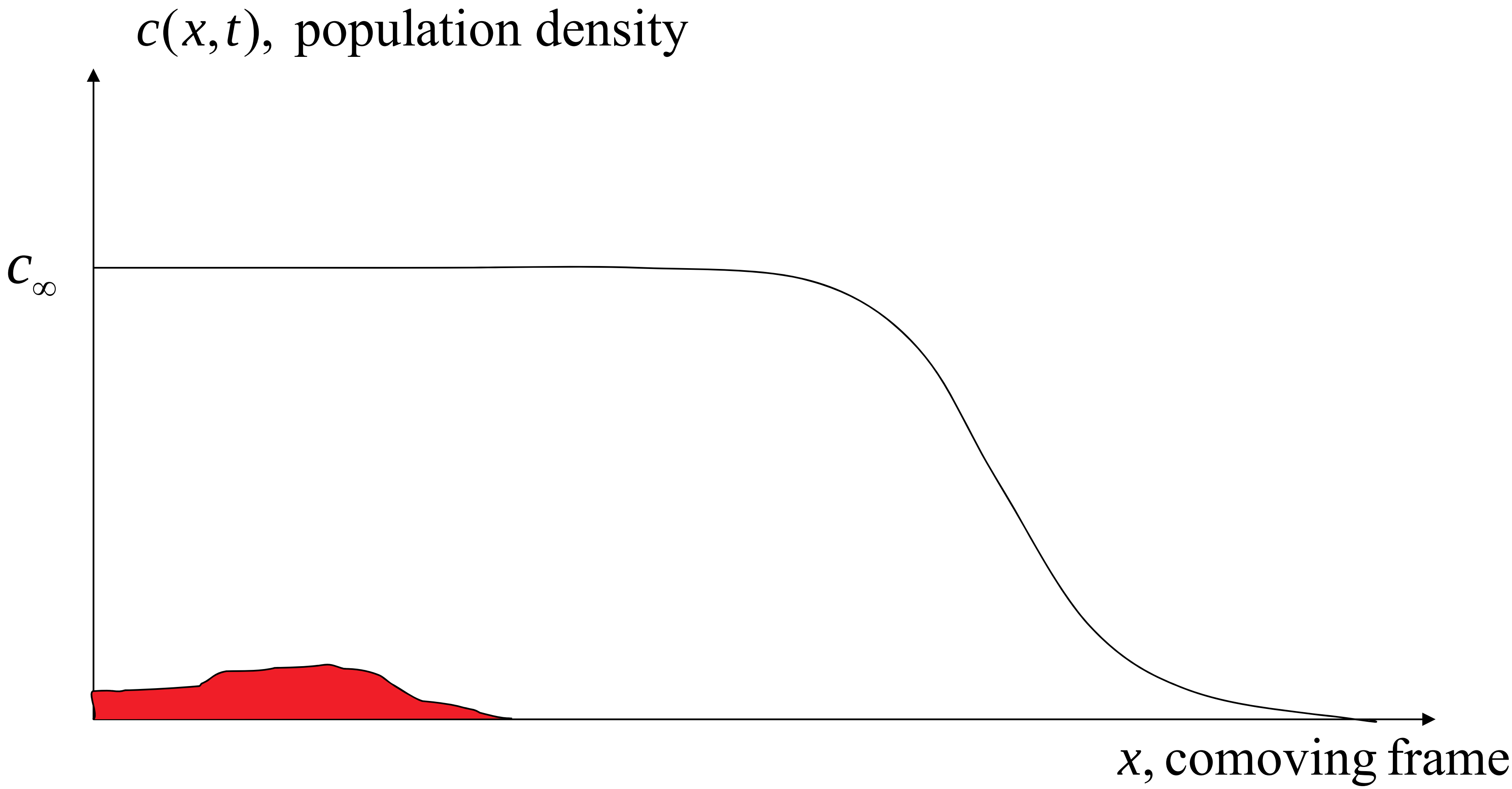
Often however …



Often however …

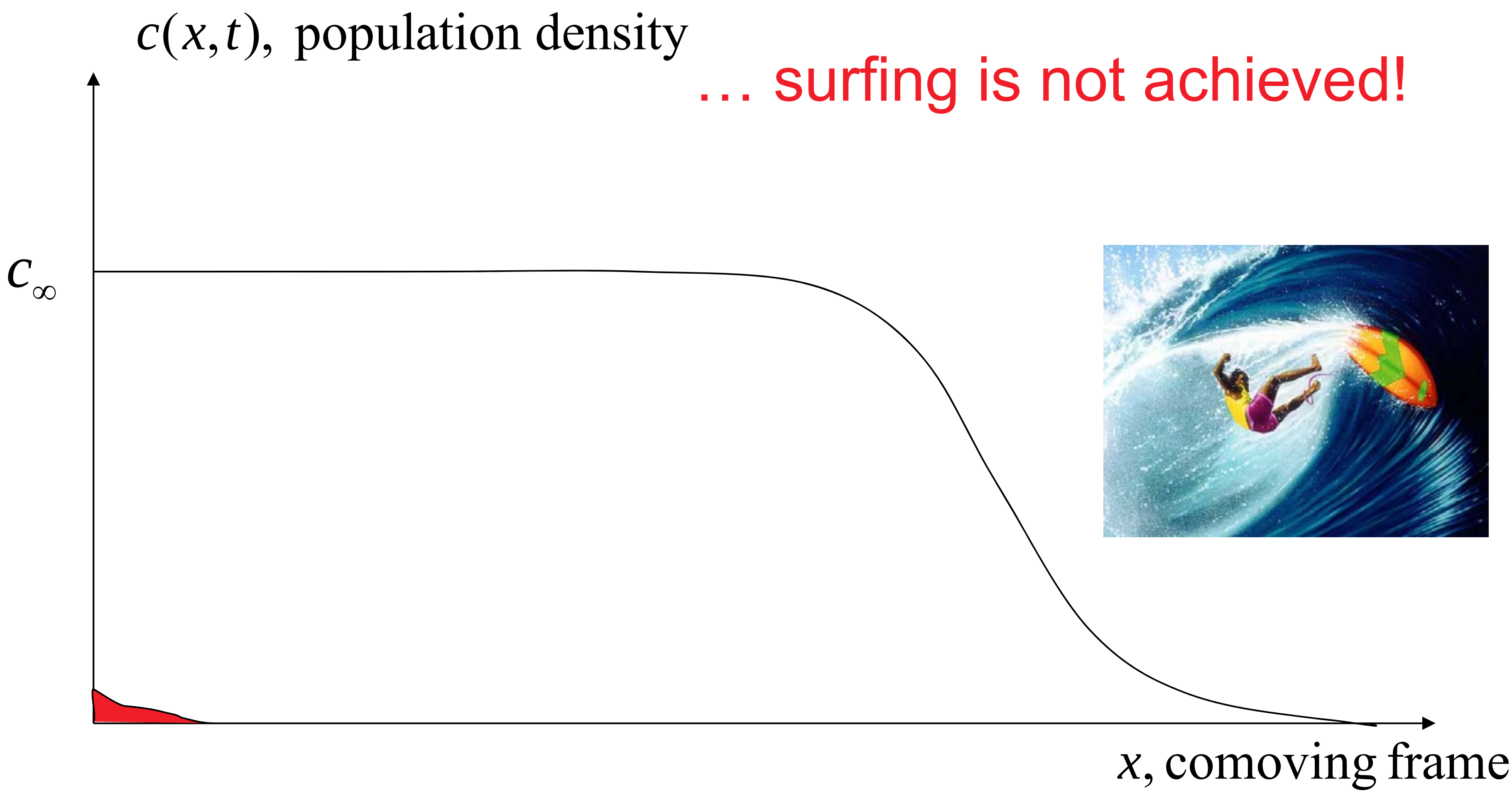


Often however …



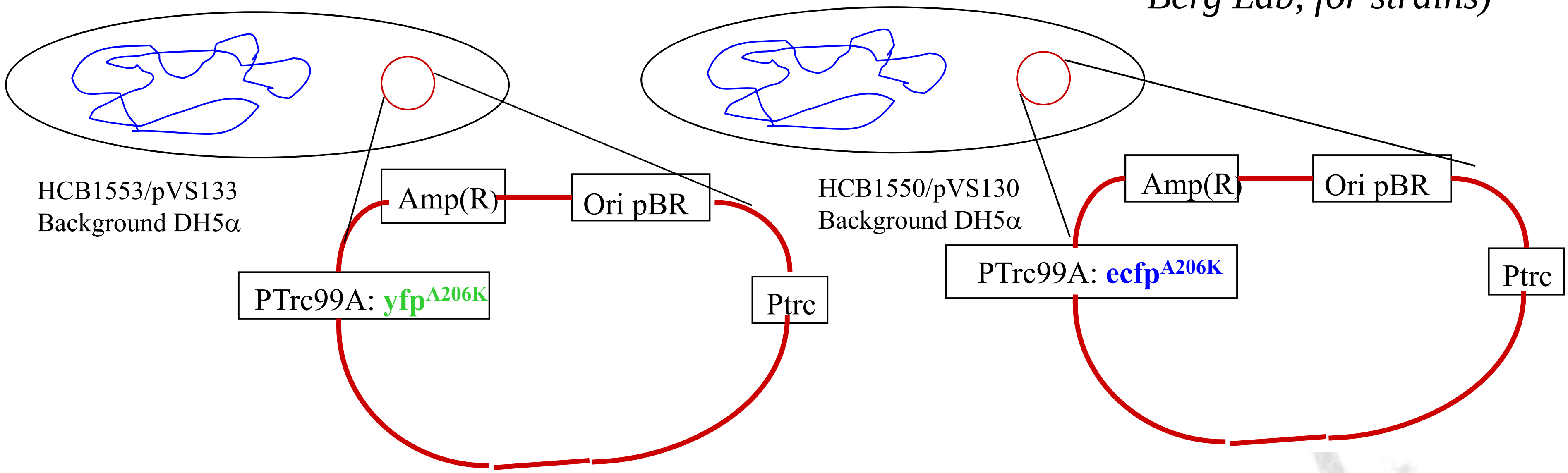
Often however …

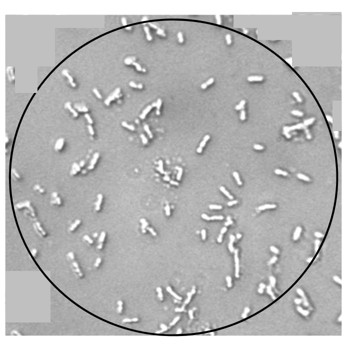
… surfing is not achieved!



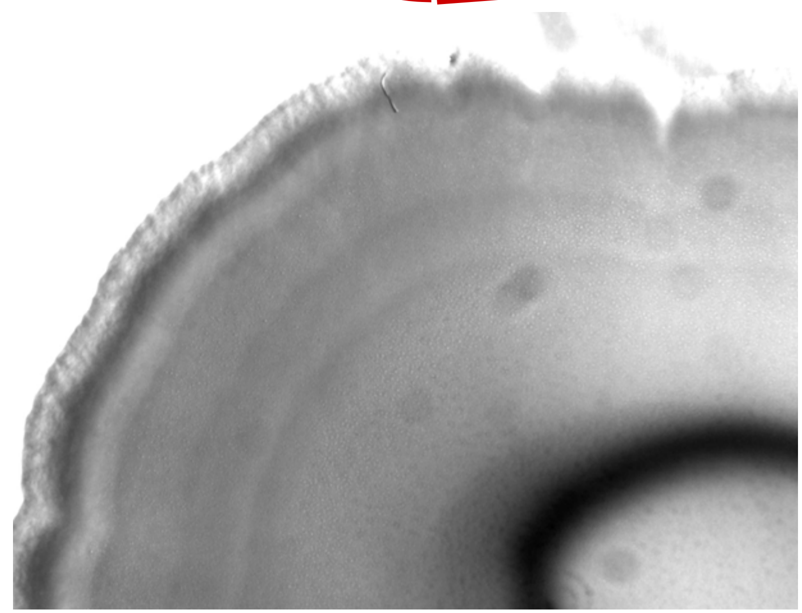
Gene Surfing in nonmotile E. coli

(thanks to Tom Shimizu, Berg Lab, for strains)





50-50 mixture,
1550/1553



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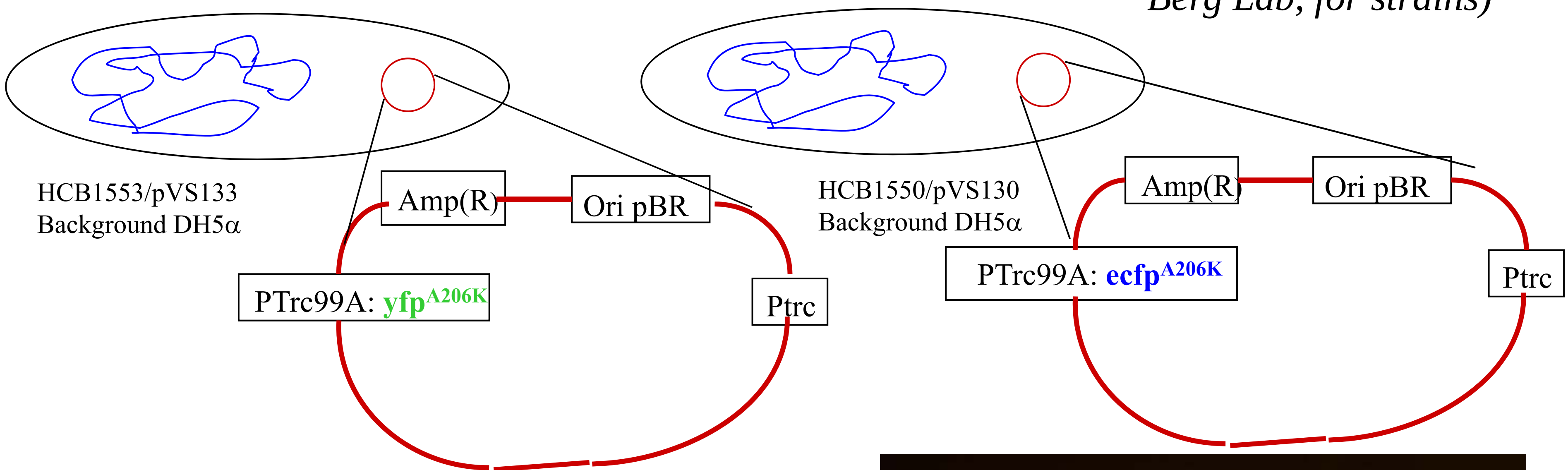

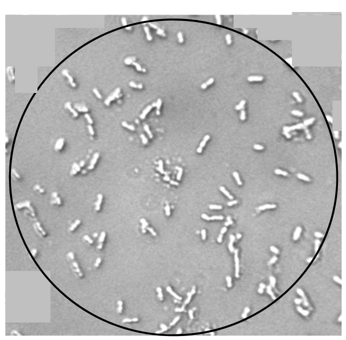

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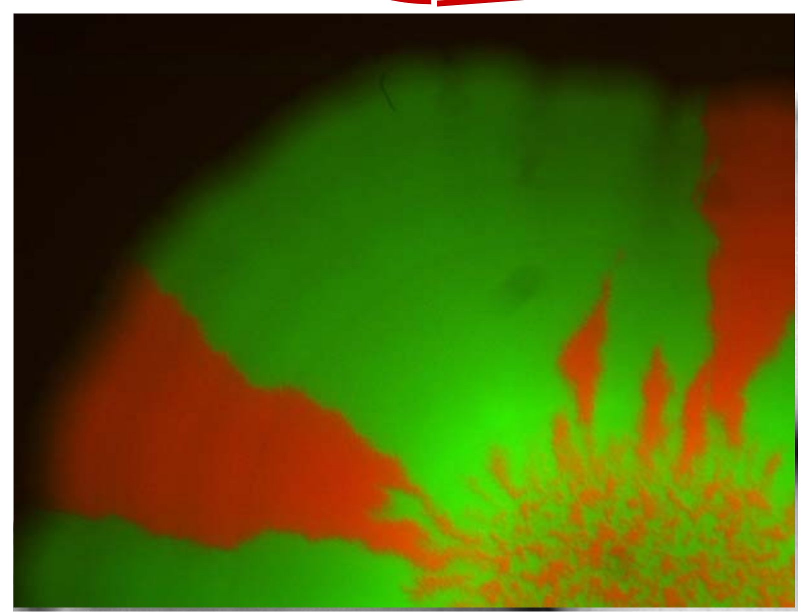
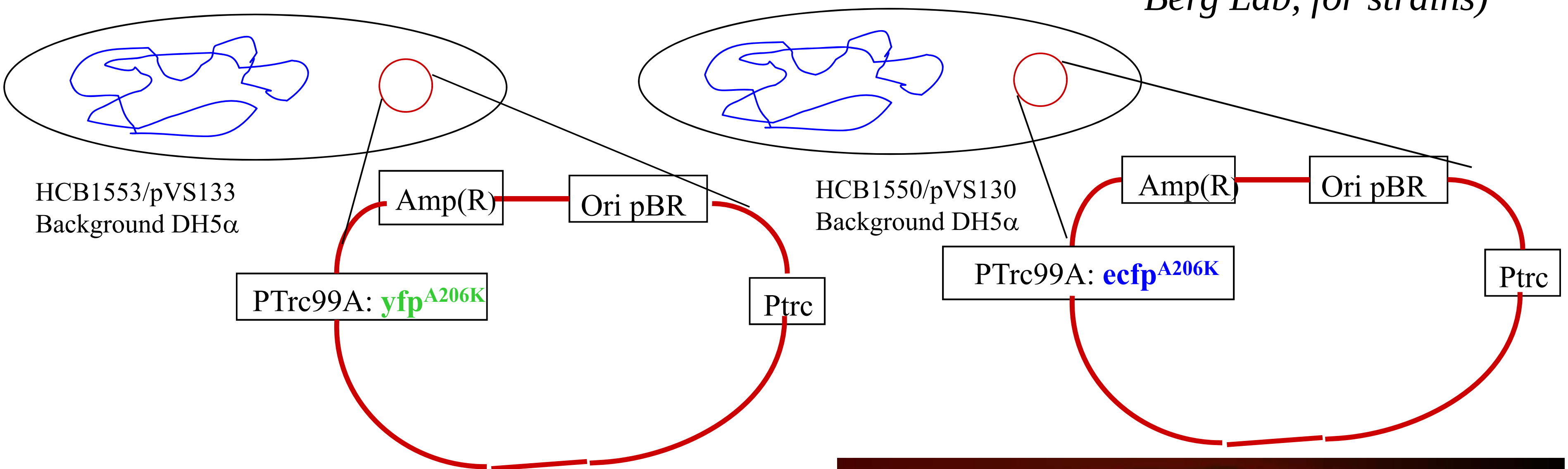
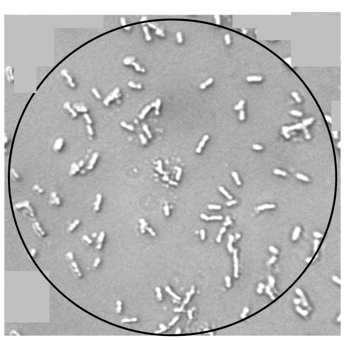


Cyan → Red

Genetic demixing in non-motile E. coli

(thanks to Tom Shimizu, Berg Lab, for strains)





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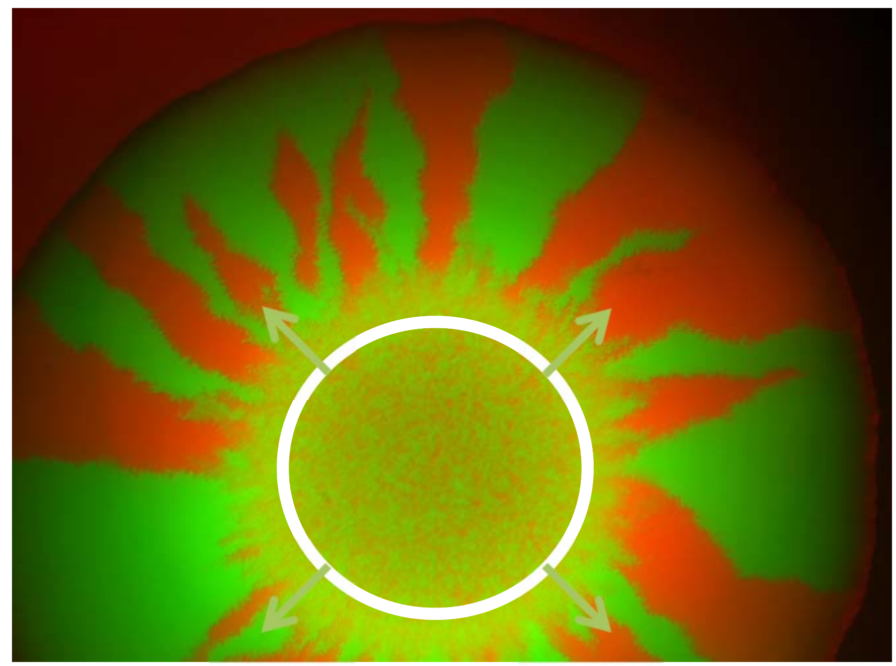
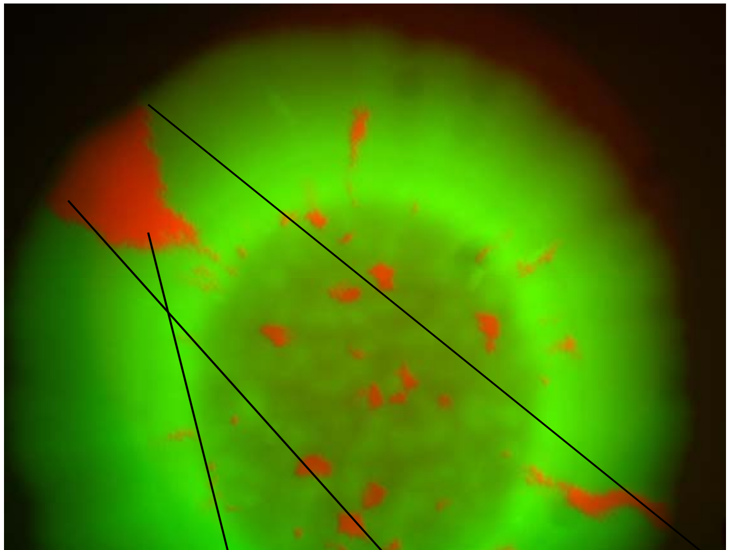
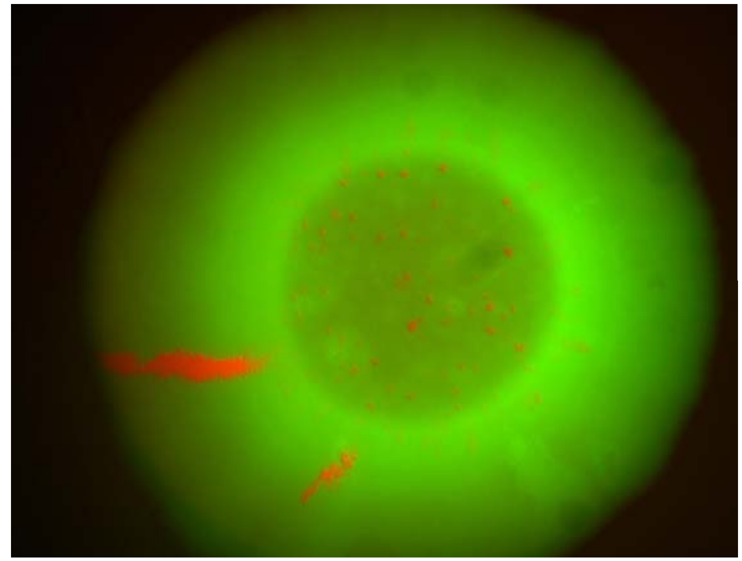


Cyan → Red

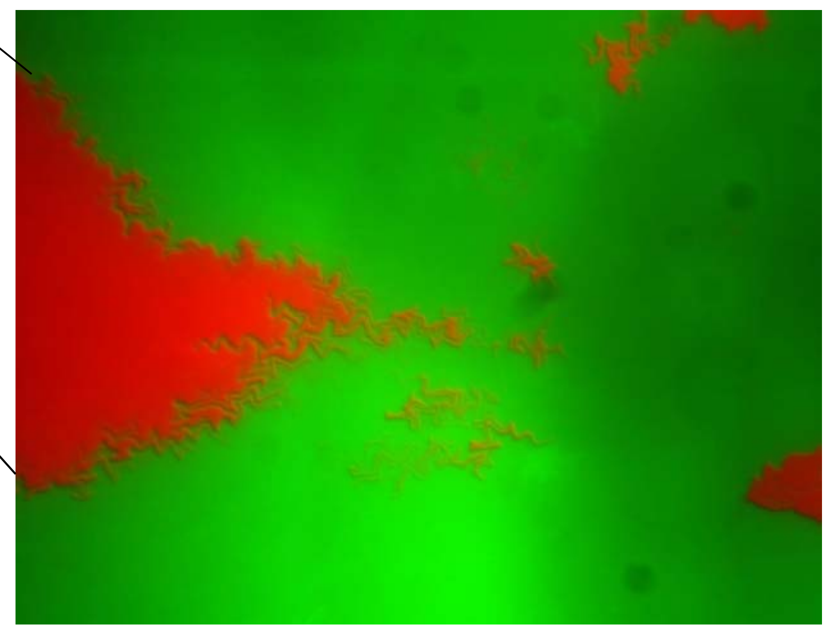
Gene surfing in the dilute limit: “survival of the luckiest”



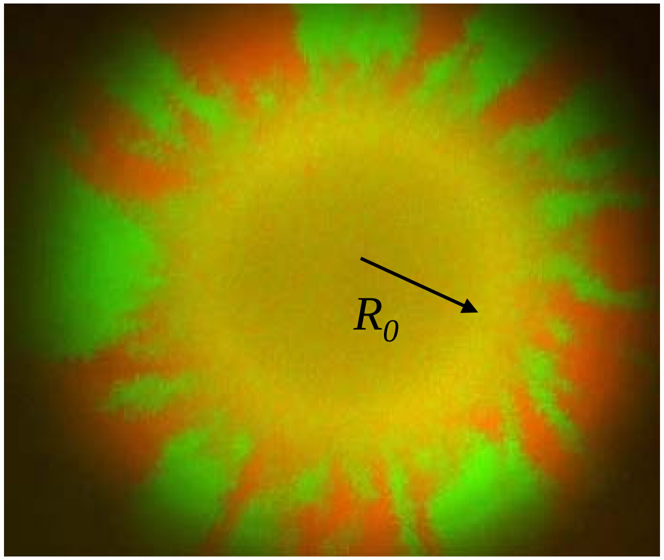
95%-5% mixture, founder population ~ 500

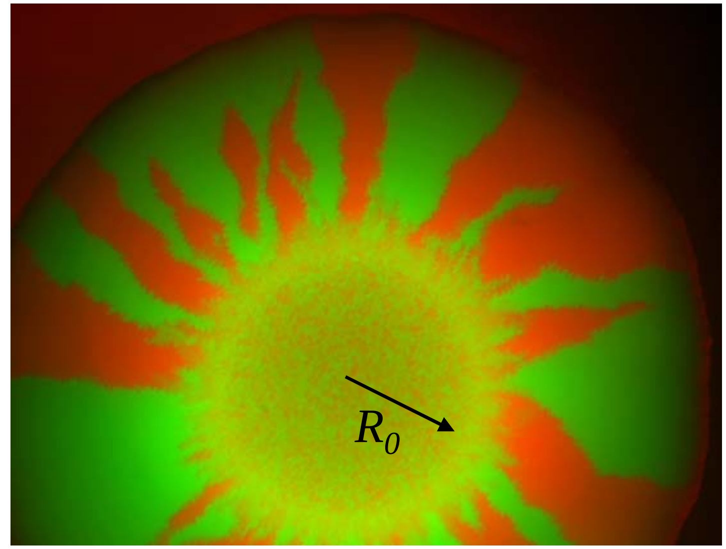


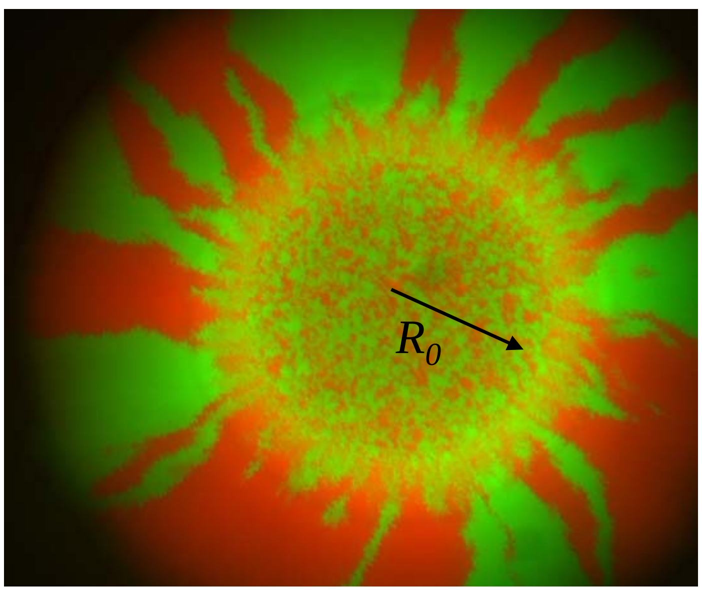
98%-2% mixture, founder population ~ 5000



What would happen if we could "replay the tape of life"?



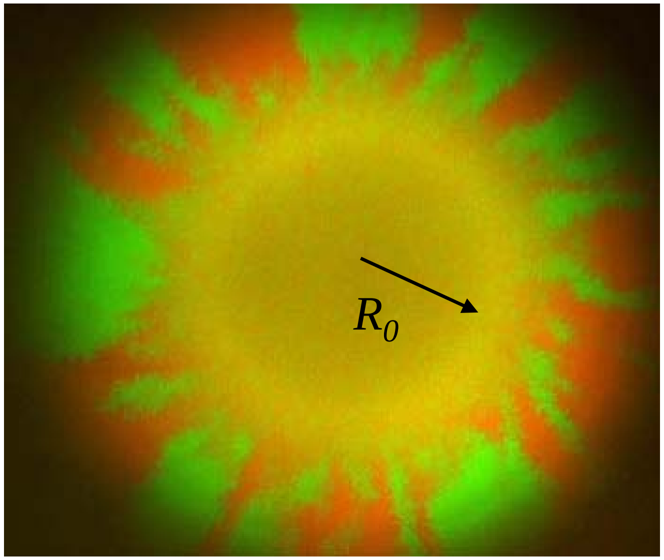


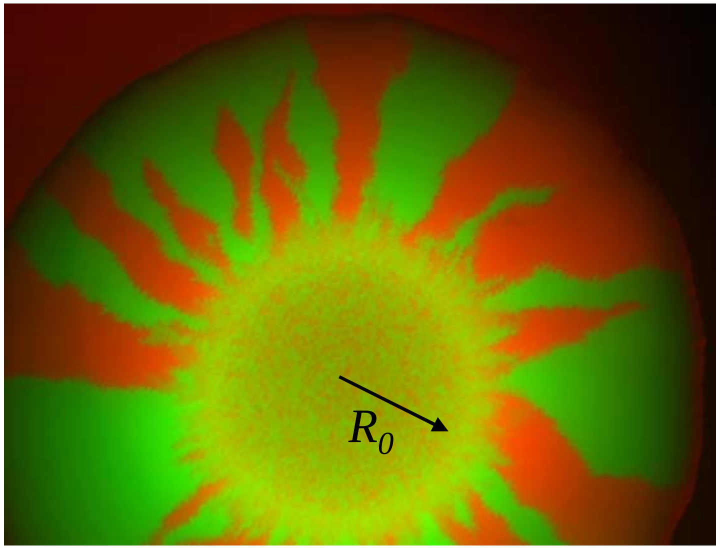


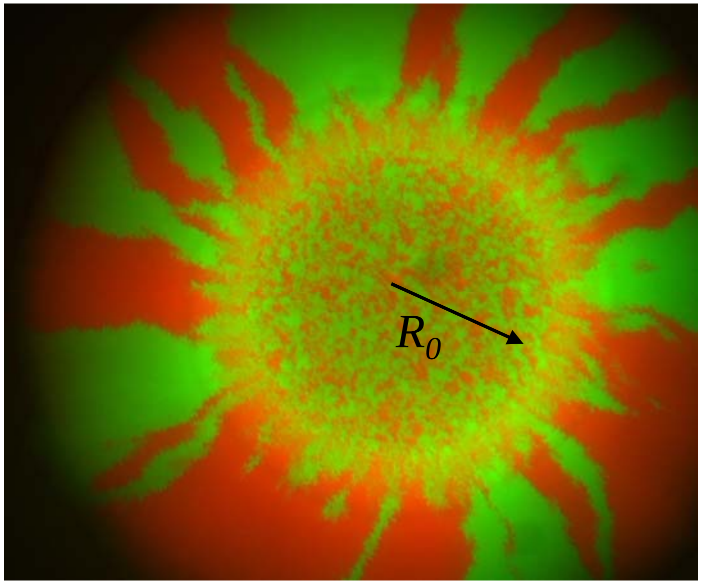
E. coli range expansions: can infer the radius R_0 of the homeland from data at the boundary:

$$N_{\mathrm{sec}} = \sqrt{\pi R_0 v / 2D_W}$$

What would happen if we could "replay the tape of life"?

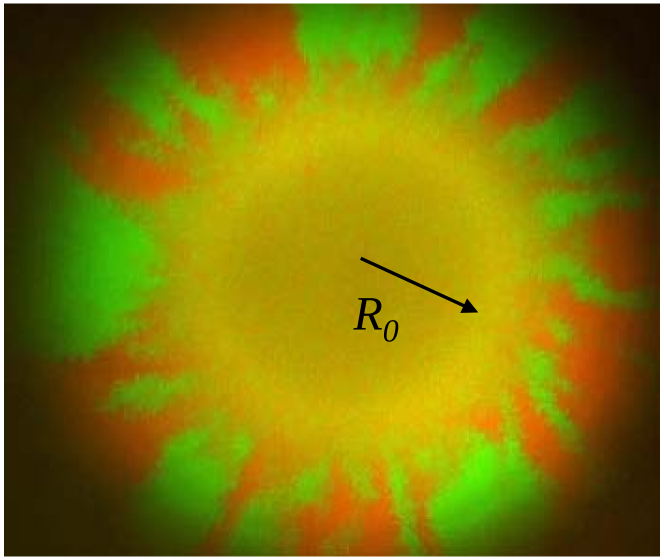


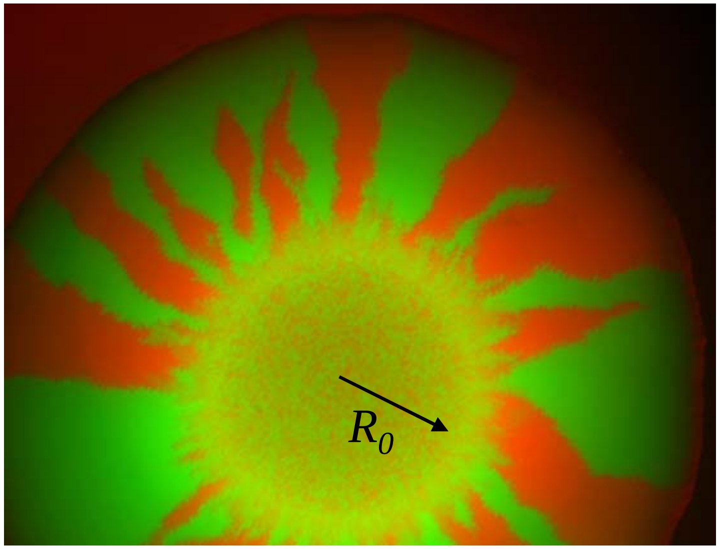


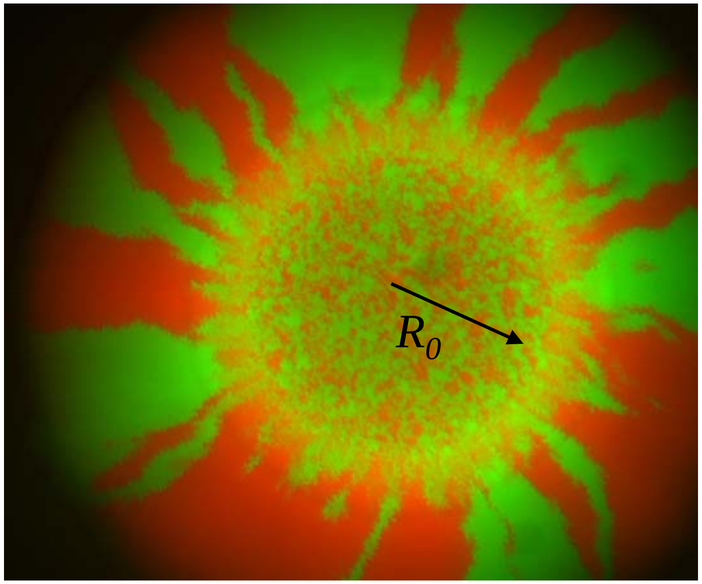


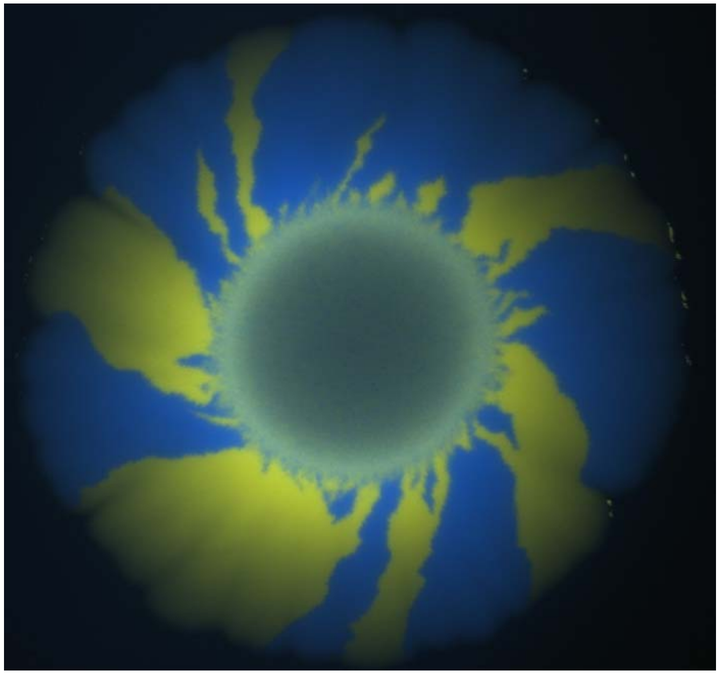
"Survival of the luckiest"

What would happen if we could "replay the tape of life"?





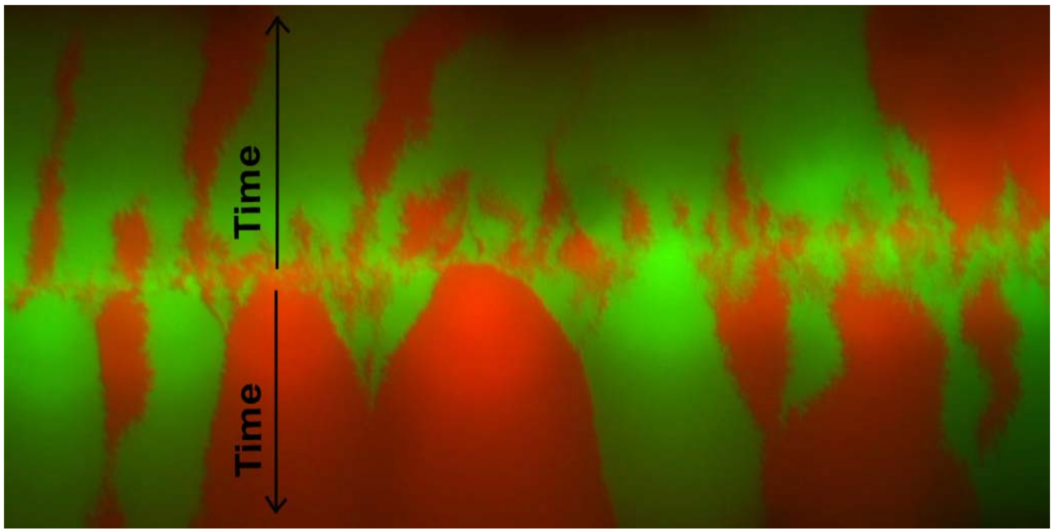




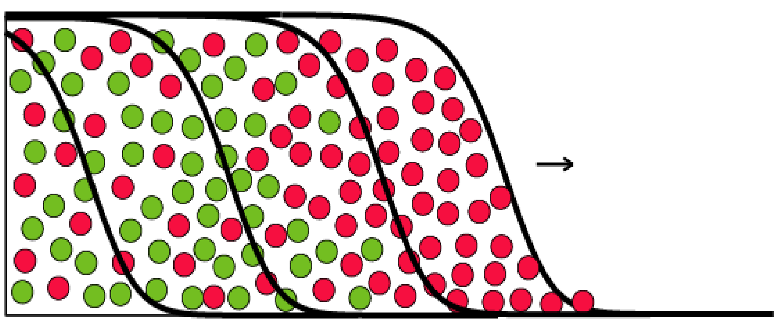
Chiral range expansions

Linear Inoculations: "Genetic demixing" results from number fluctuations at the frontier

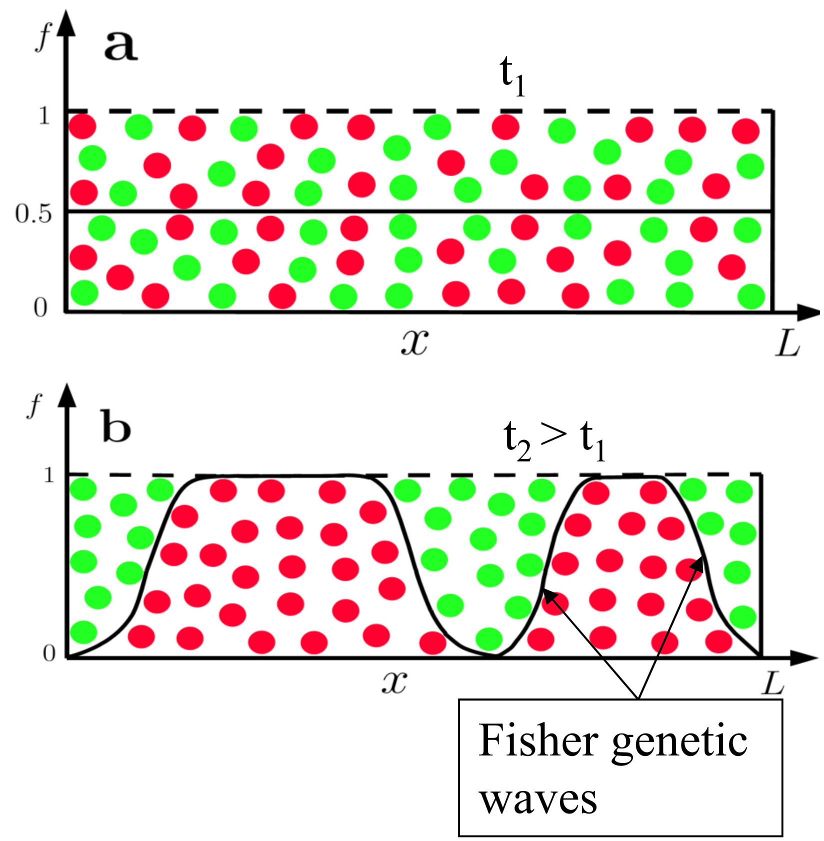
View from the top: razor blade innoculation



Side view as the population wave advances:



View of a "dust mote" on a Petri dish as the wave advances….



Thank you!

http://streetanatomy.com