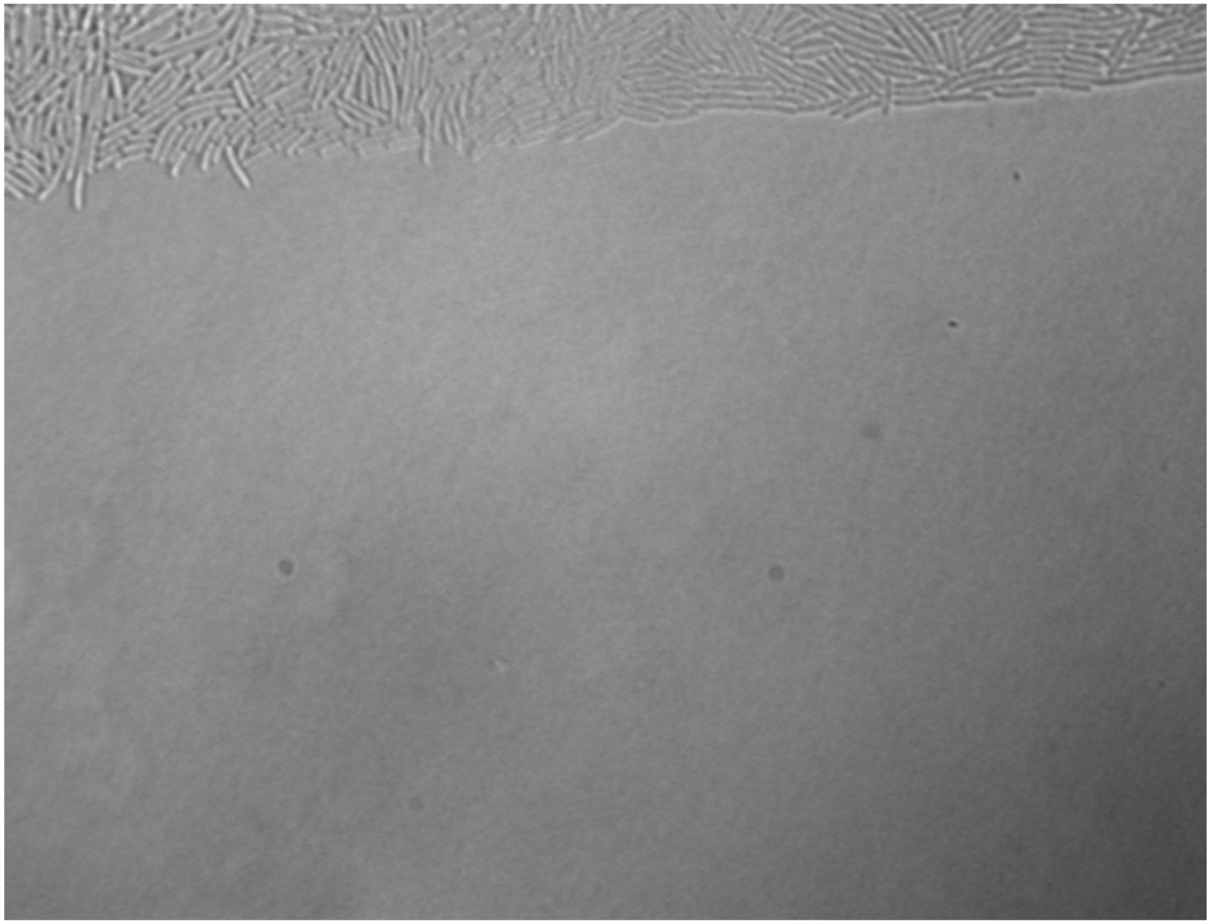
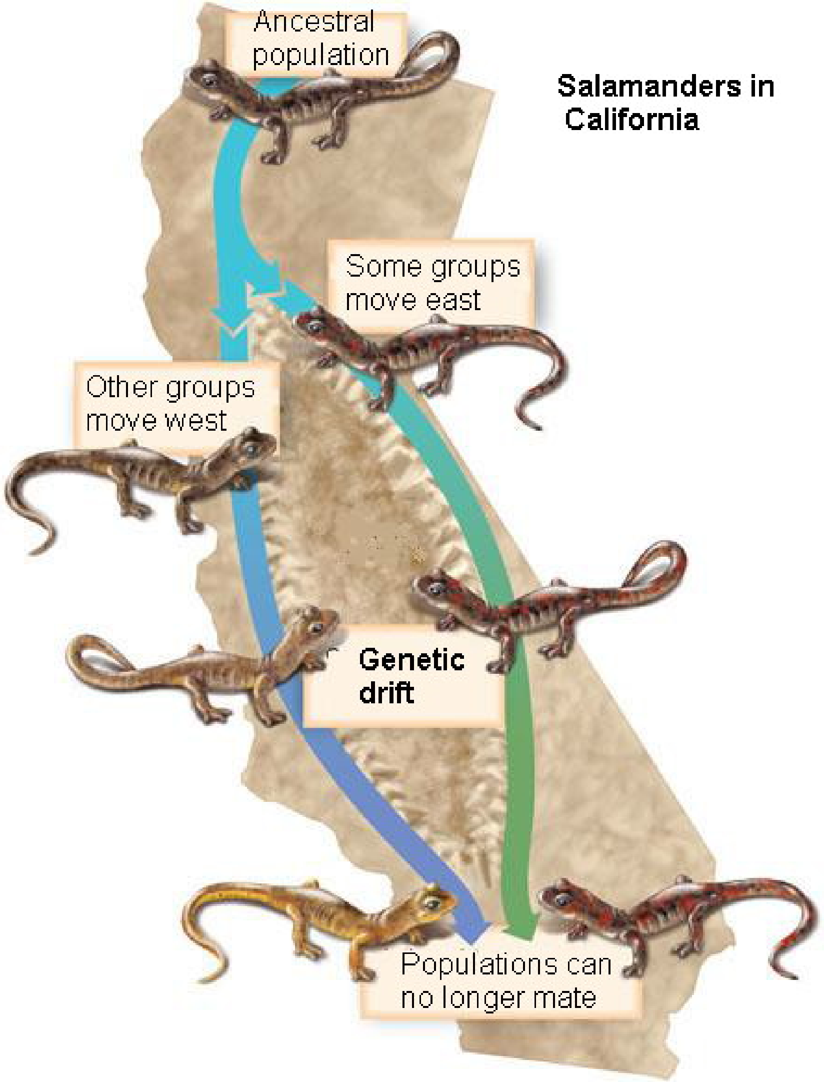
Range expansions can be unstructured or structured



unstructured range expansion
(E. coli on a Petri dish, O. Hallatschek & drn Ramanathan lab)

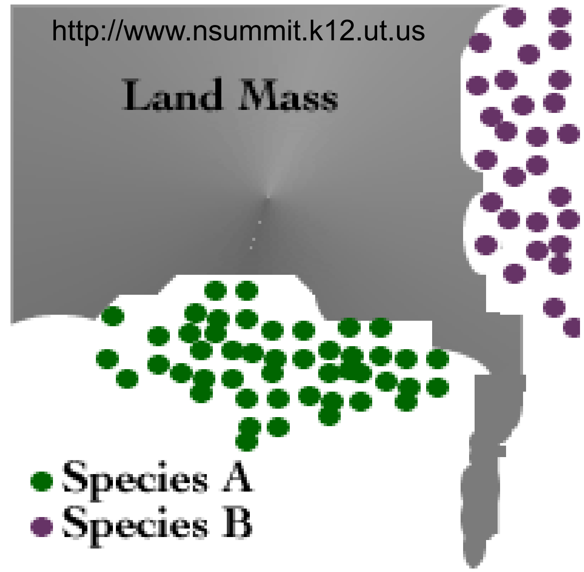
http://legacy.hopkinsville.kctcs.edu



structured range expansion
(leads to allopatric speciation)

Collective Behavior and Growth:

Range Expansions in Structured Environments



Frontier populations with spatial structure

-- Our world is not featureless landscape → geographical features influence ecosystems and population fronts

-- How does a range expansion in a inhomogeneous environment shape genetic diversity at the frontier?

Simplified model of spatial structure: migration around obstacles such as "lakes and deserts" (or a mountain range…)

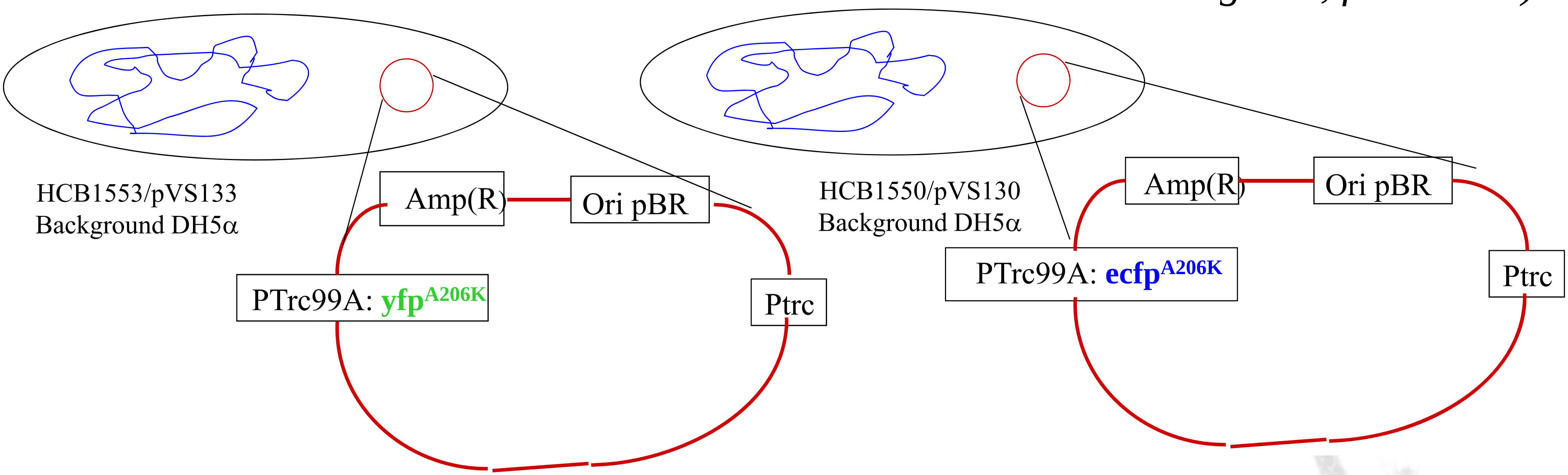
-- Population fronts around obstacles: experiments, "Fermat's principle" and simulations of the bacterial virus T7 invading inhomogeneous bacterial lawns

---Adding population genetics: simulations and an experiment with E. coli

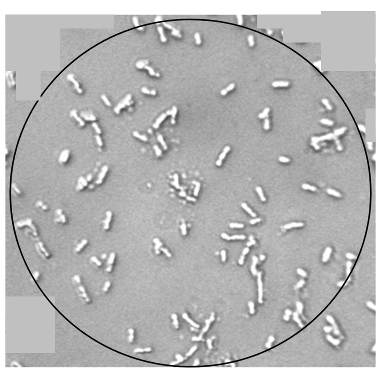
Wolfram Moebius

Andrew Murray

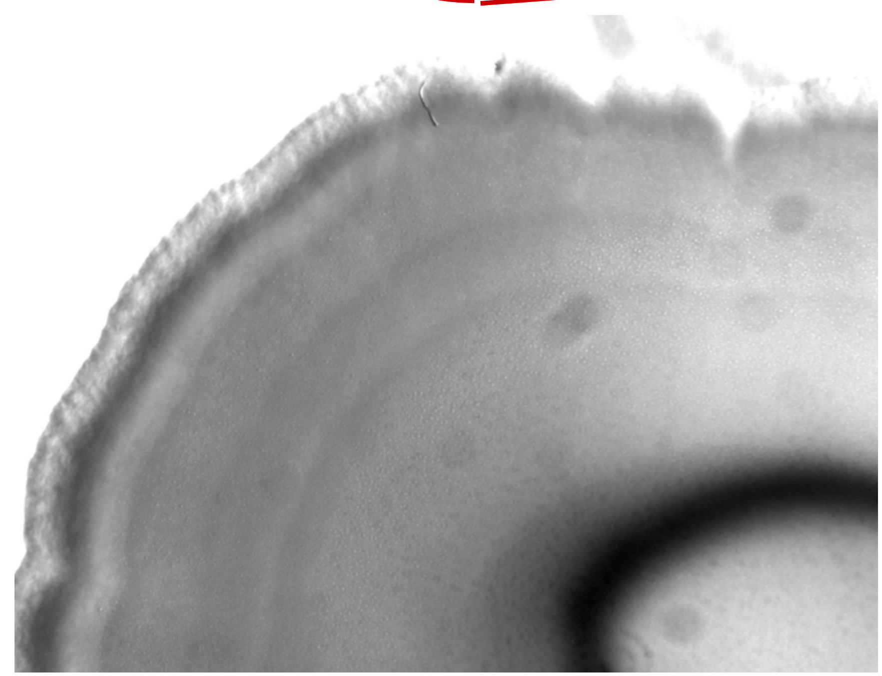
Unstructured range expansion in non-motile E. coli *(thanks to Tom Shimizu, Berg Lab, for strains)*



O. Hallatschek, drn et al., PNAS **107**,19926 (2007)



50-50 mixture,
1550/1553



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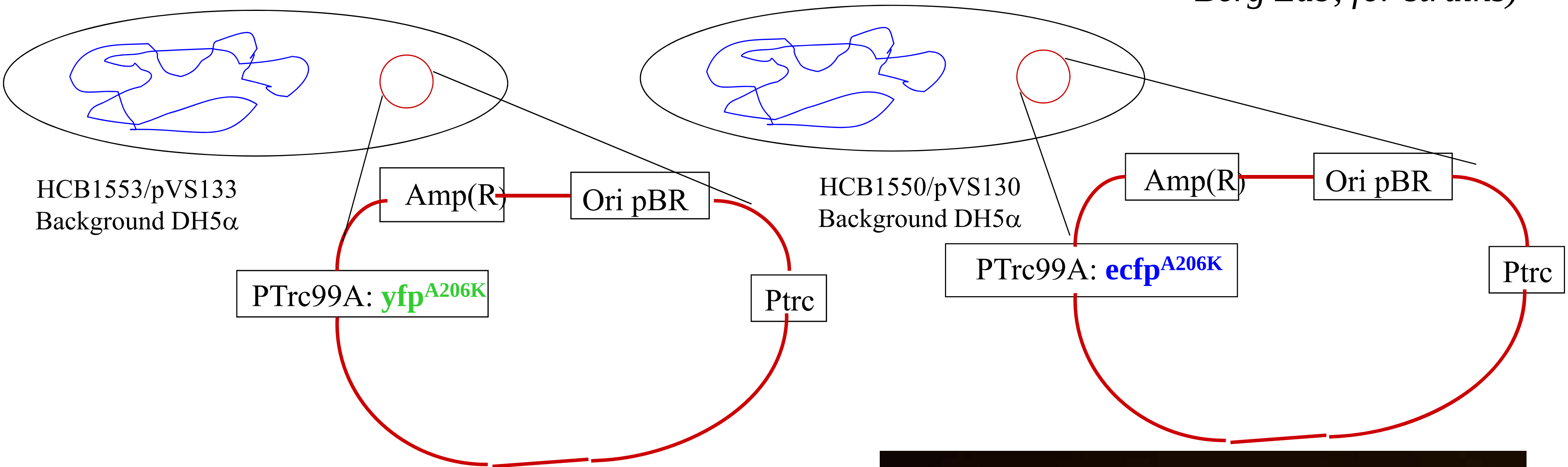
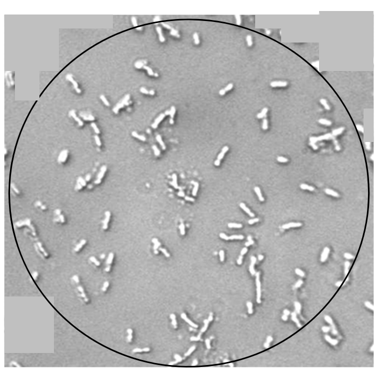


O. Hallatschek, drn et al., PNAS **107**,19926 (2007)



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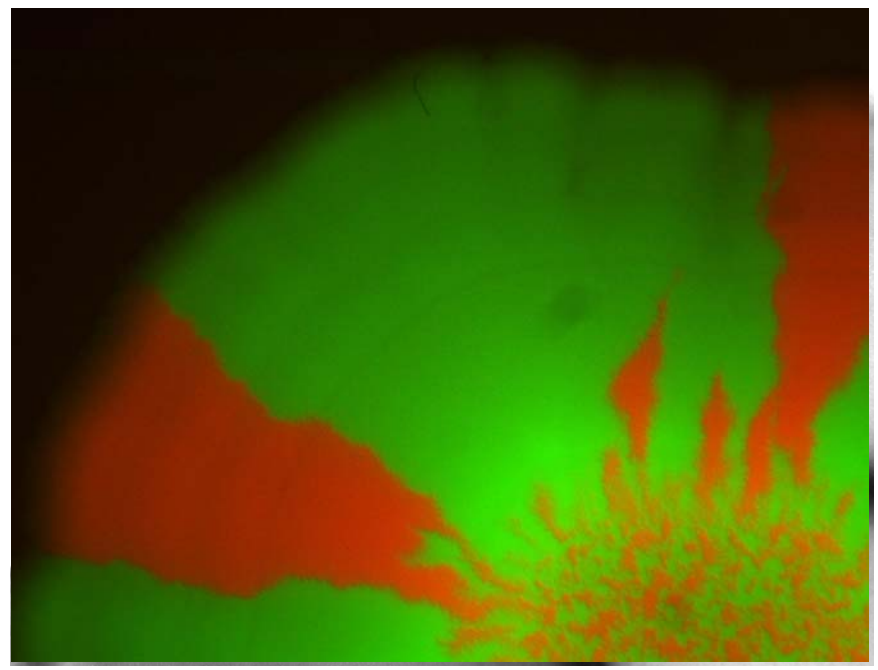
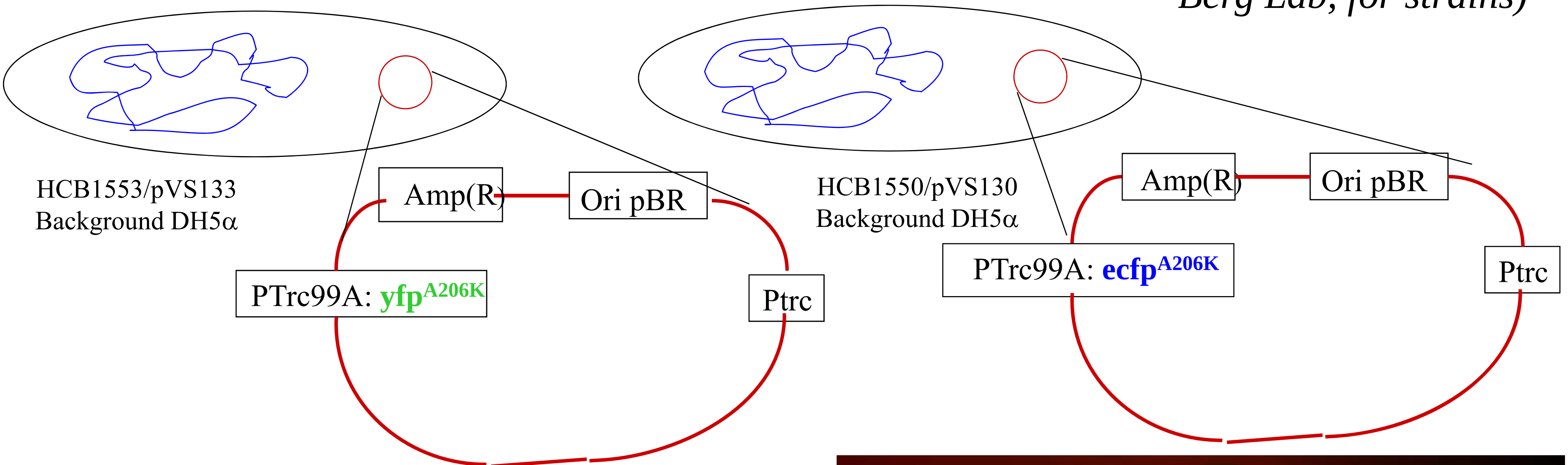
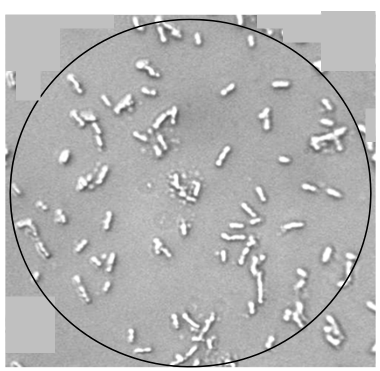


Cyan → Red

Unstructured range expansion in non-motile E. coli

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





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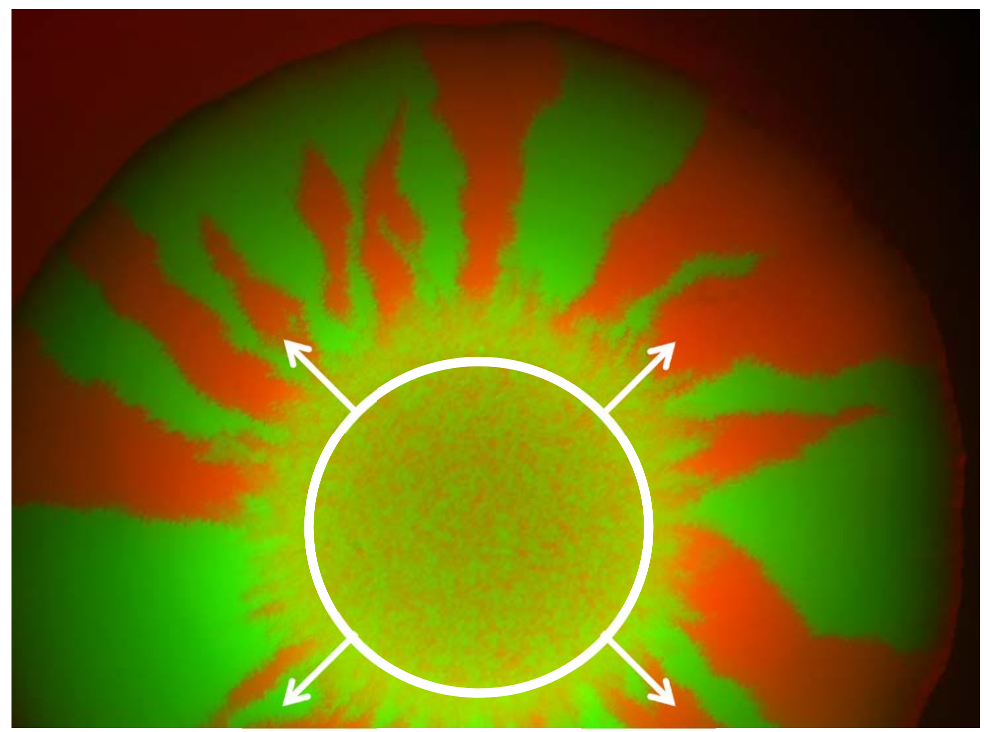
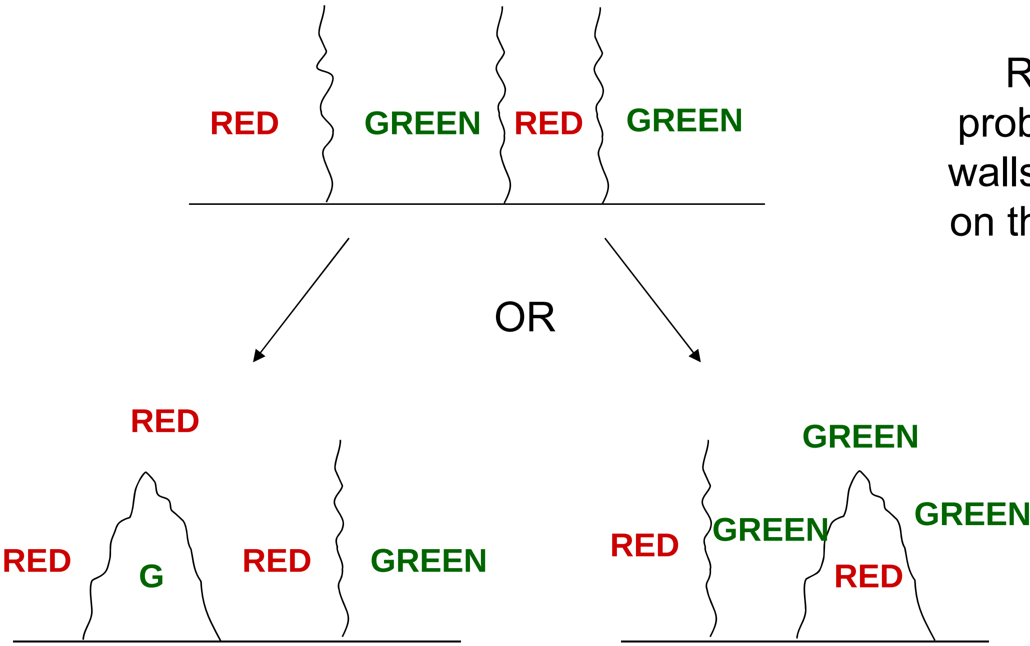
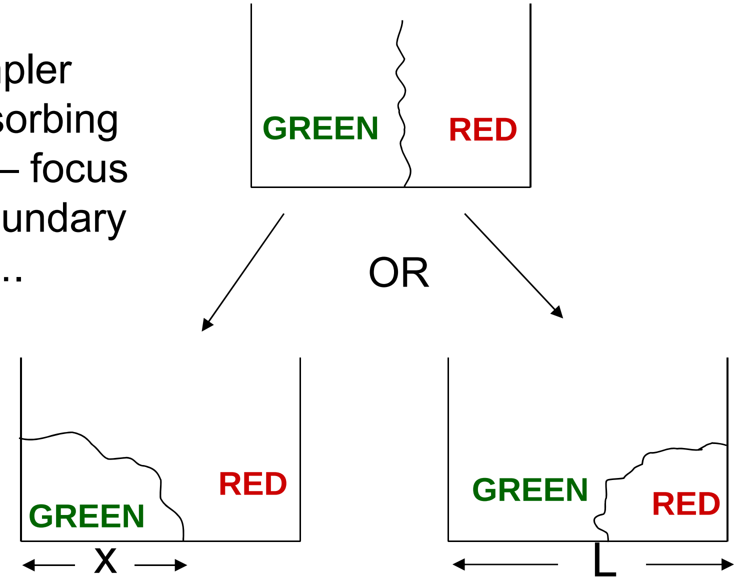


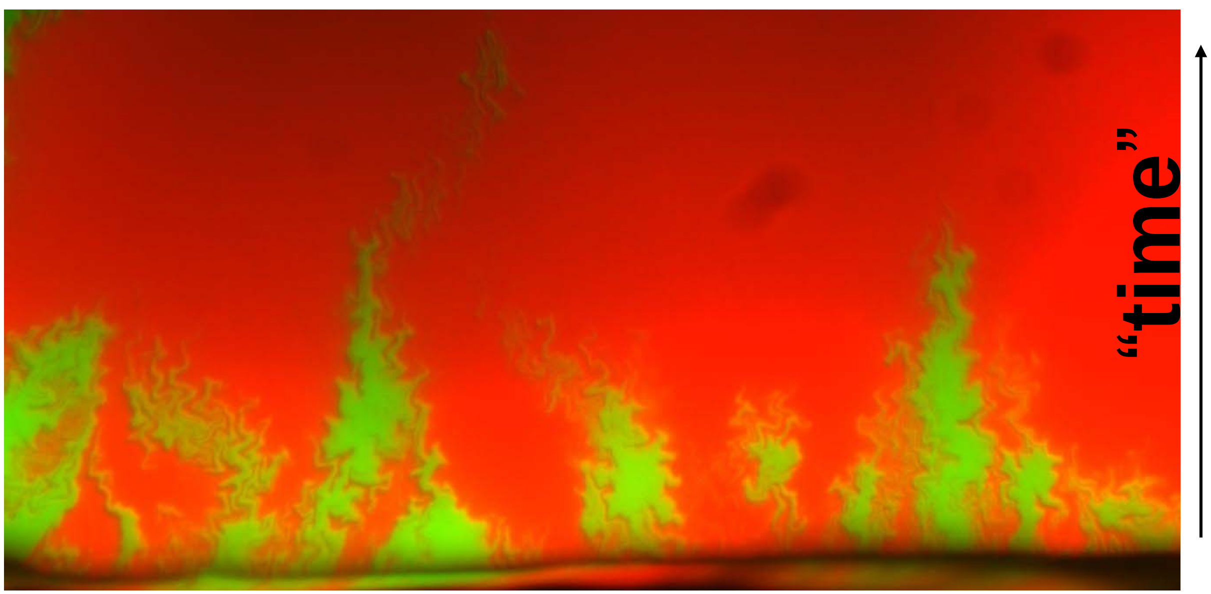
Cyan → Red

Approximate linear inoculations by annihilating random walks



Replace with simpler problem of rigid absorbing walls on either side – focus on the fate of the boundary in the middle….





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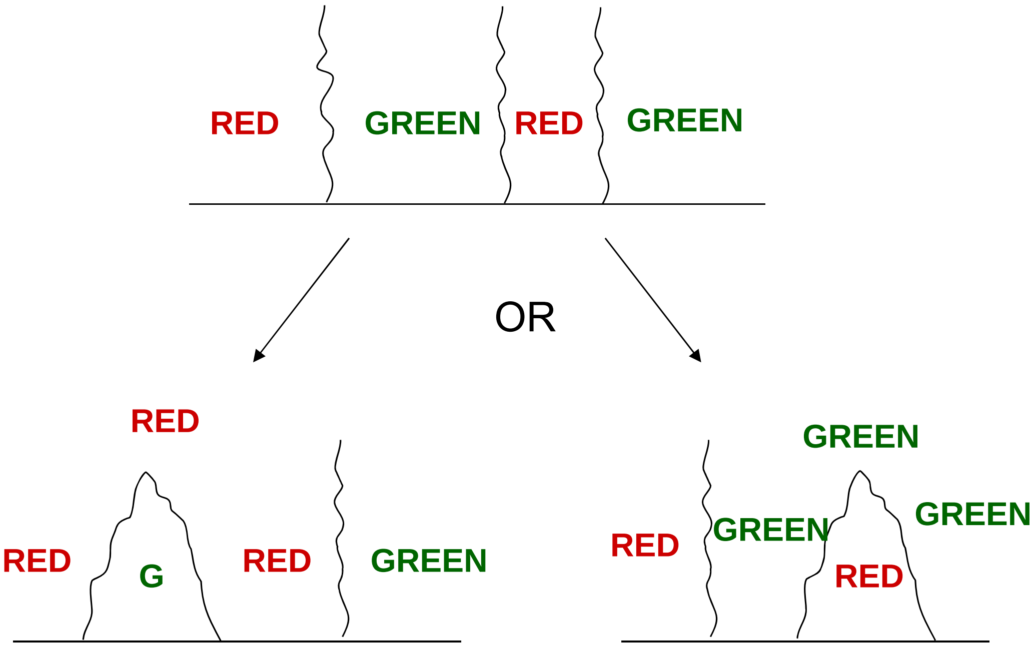
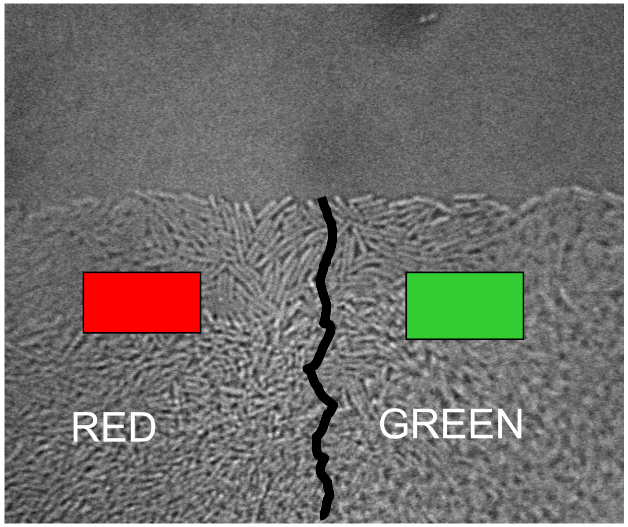
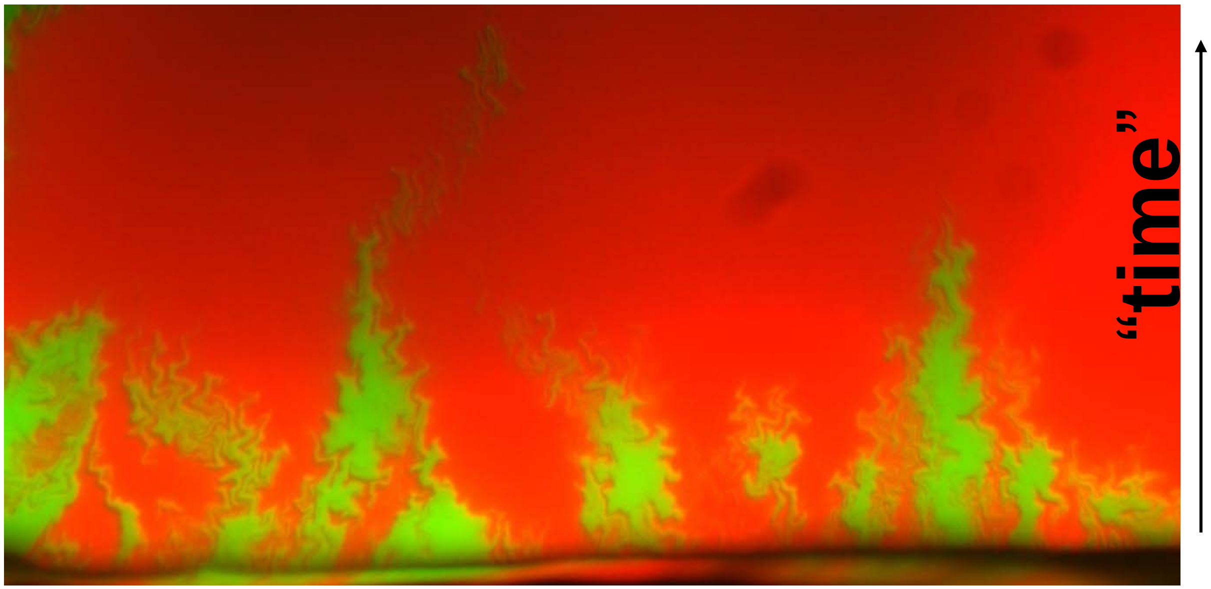


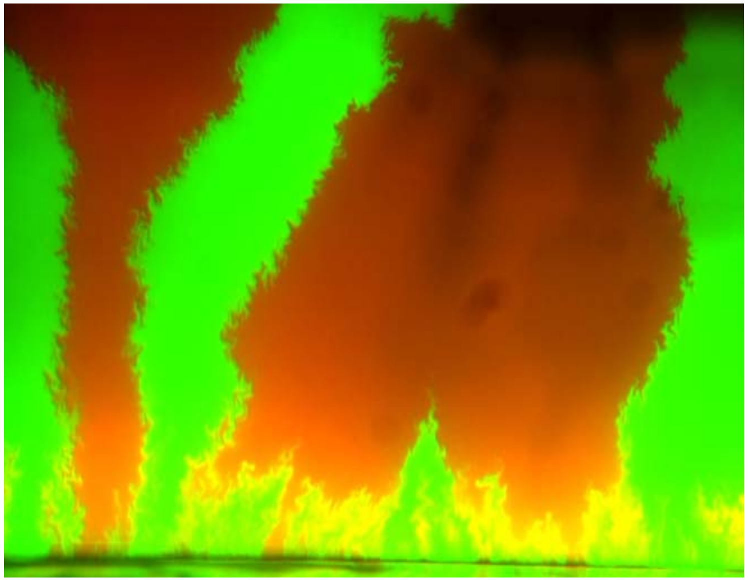




If D_W = *wall diffusion constant*

$$n_w(t) = \text{density of walls}$$
$$= 1/\sqrt{2D_W t}$$
$$\propto 1/t^{\zeta}, \text{ in general}$$

But the genetic boundaries may wander more vigorously…

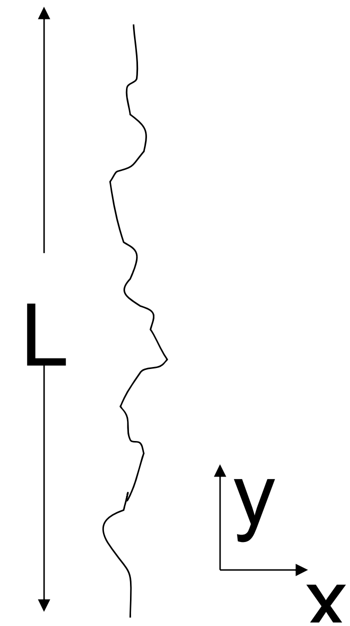


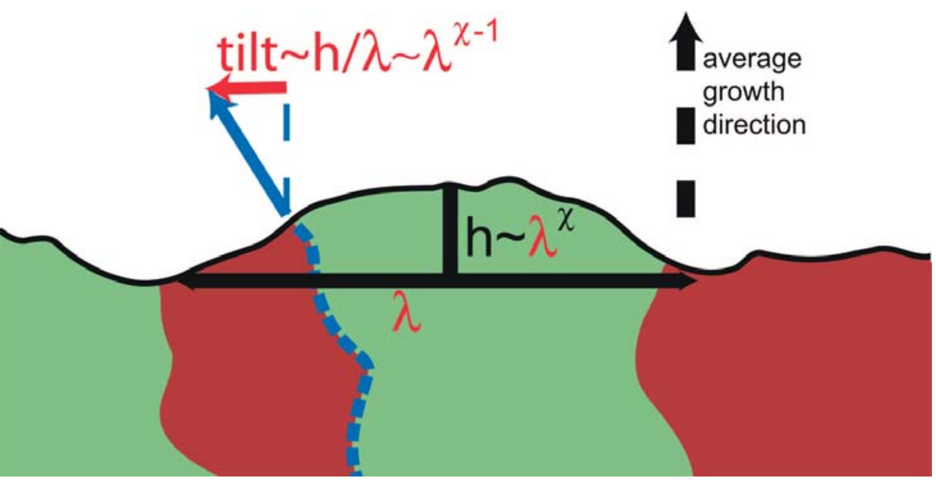
$$< [x(L) - x(0)]^2 > \quad \approx const. \times L^{2\zeta}$$

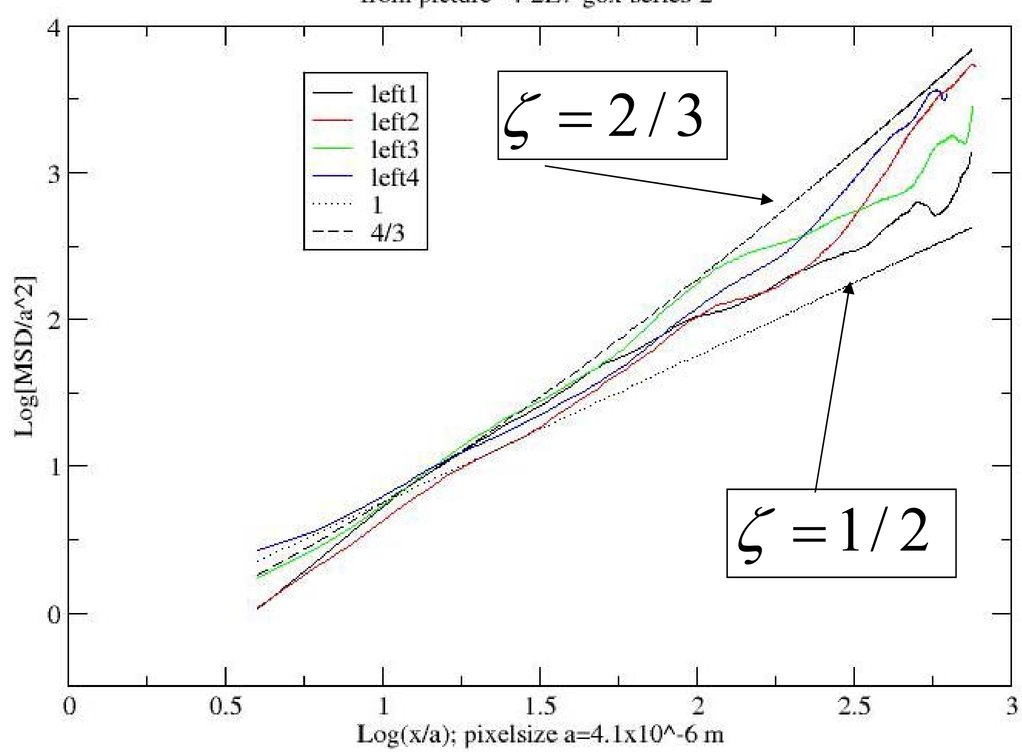
$\zeta = 1/2,$ random walk

$\zeta = 1 + (\chi - 1)/z = 2/3,$

(KPZ, χ=1/2, z=3/2)

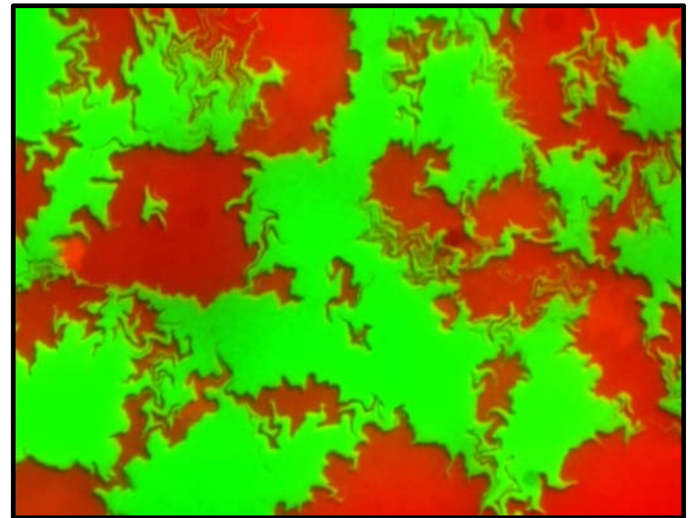






Hallatschek, Hersen, Ramanathan, drn, PNAS **104,** 19926 (2007)

How can we make structured environments? Can the "homeland" be regarded as an "ecological landscape"?

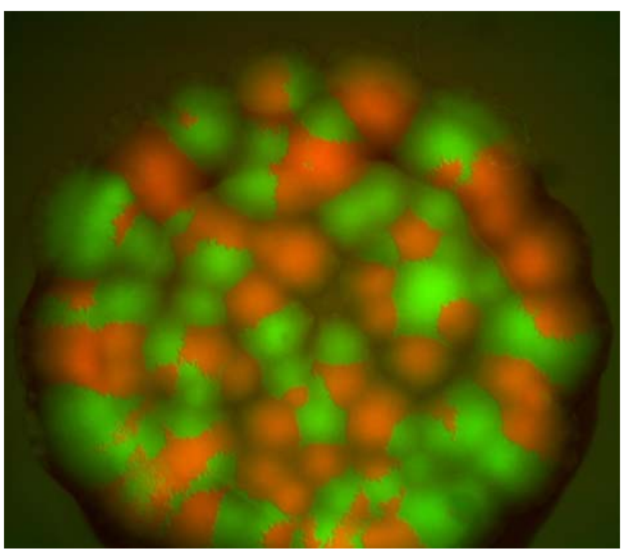


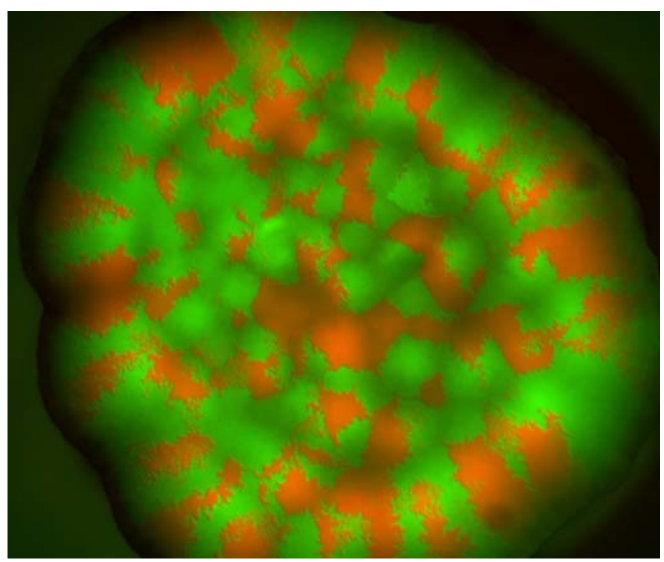
50-50 circular inoculants 24 hours after inoculation; (~ 1mm spot size)

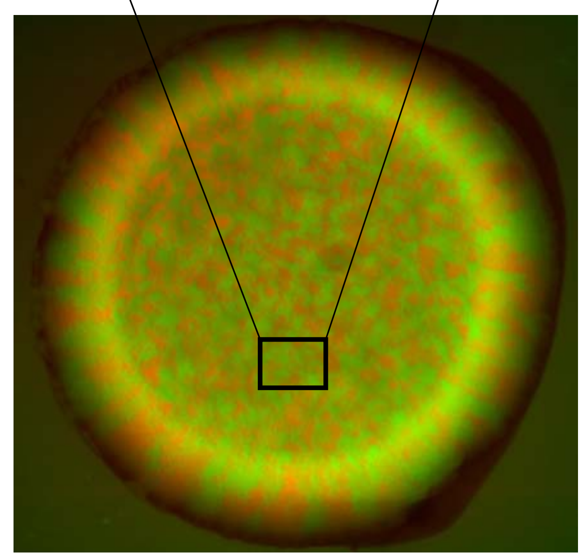
~25 green & 25 "red" viable founder bacteria

~250 green & 250 "red" viable founder bacteria

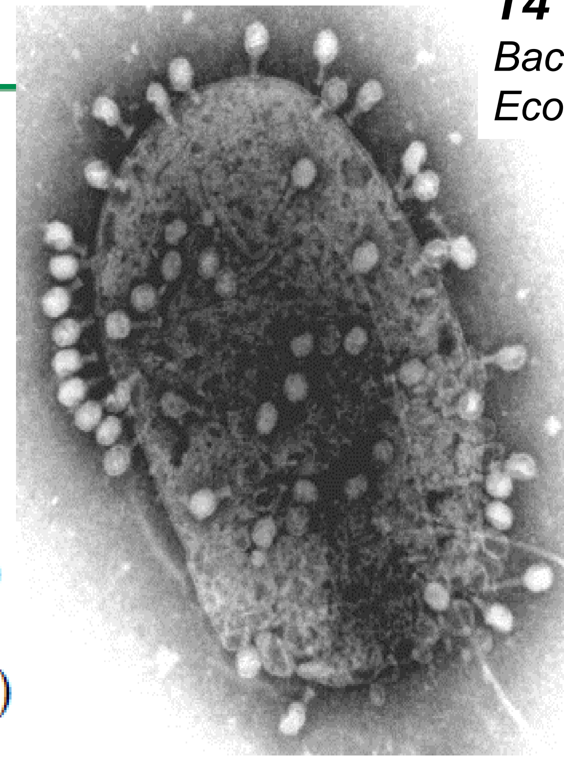
~2500 green & 2500 "red" viable founder bacteria







Introduction - bacteriophage T7



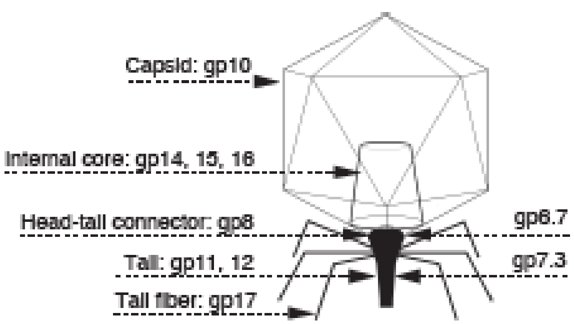
T4 infection
Bacteriophage Ecology.aspx

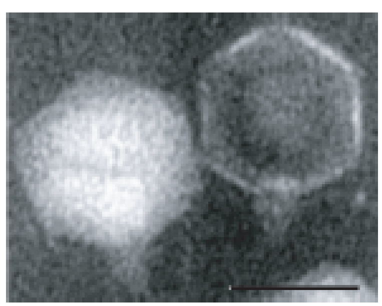
- phage T7: well-studied
- obligatory lytic
- forms large plaques
- grows on bacteria in stationary phase

- size: ~ 60 nm (1/20 *E. coli* size)
- 40 kb linear genome (length can be moderately changed)
- 56 known or potential genes,
  three classes of genes (early, metabolism, morphogenesis)

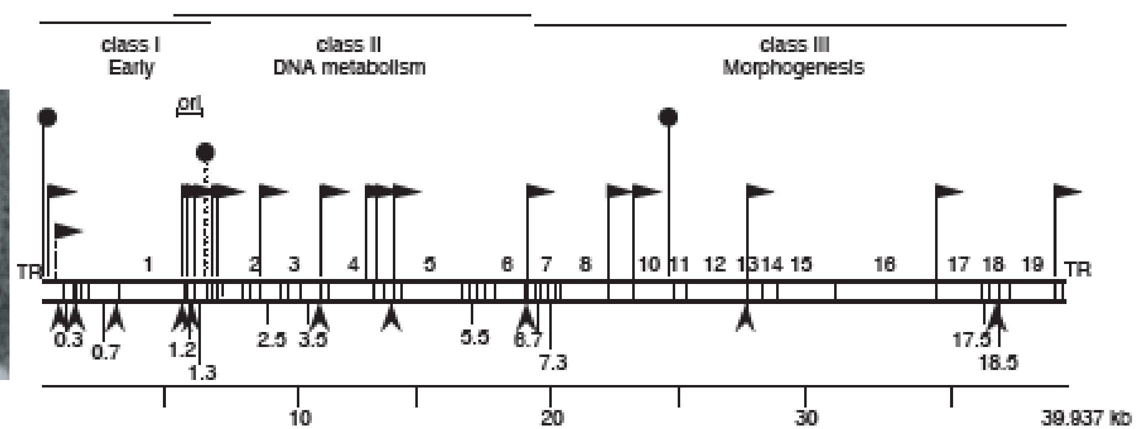
- early genes transcribed by *E. coli* RNAP, importantly: gene 1, coding for T7 RNAP
- other genes transcribed by T7 RNAP

[figures from review by Ian J. Molineux]





phage T7 genome



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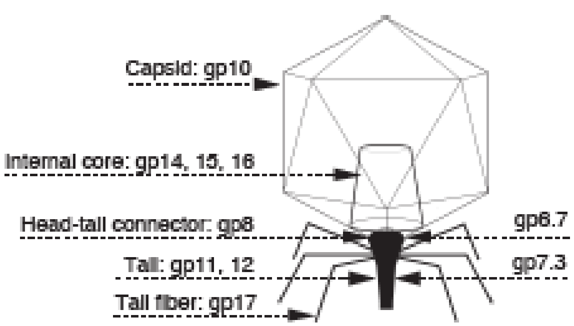

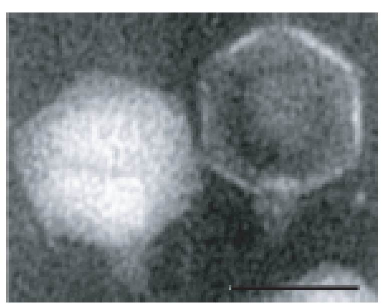

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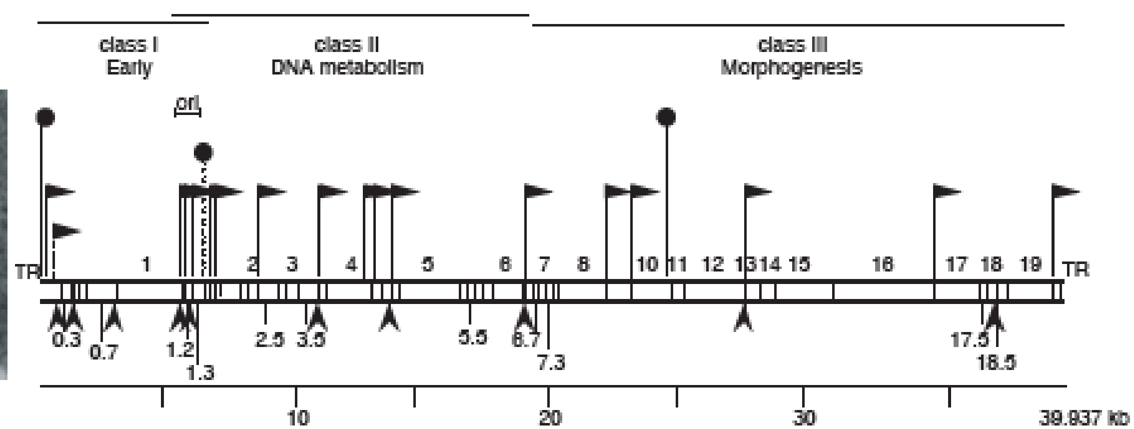


Growth of viral plaques

J. Yin and J. S. McCaskill
Biophys. J. ***61***, *1540 (1992)*

- ***A virus V encounters a bacterium B and (reversibly) produces an infected organism I***

$$V + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} I \xrightarrow{k_2} Y \cdot V$$

- ***The infected bacterium lyses in a latency time $1/k_2$ to produce new viral particles with an integer yield Y (Y ~ 30 for T7)***

- ***Reaction-Diffusion equations for [V], [B] and [I] lead to a Fisher equation for the spatial virus concentration [V] = u(r,t)***

$$\frac{\partial}{\partial t} u(\vec{r},t) = D\nabla^2 u(\vec{r},t) + a u(\vec{r},t)[1 - u(\vec{r},t)/K]$$

$K =$ phage density in the plaque $=$ "carrying capacity"

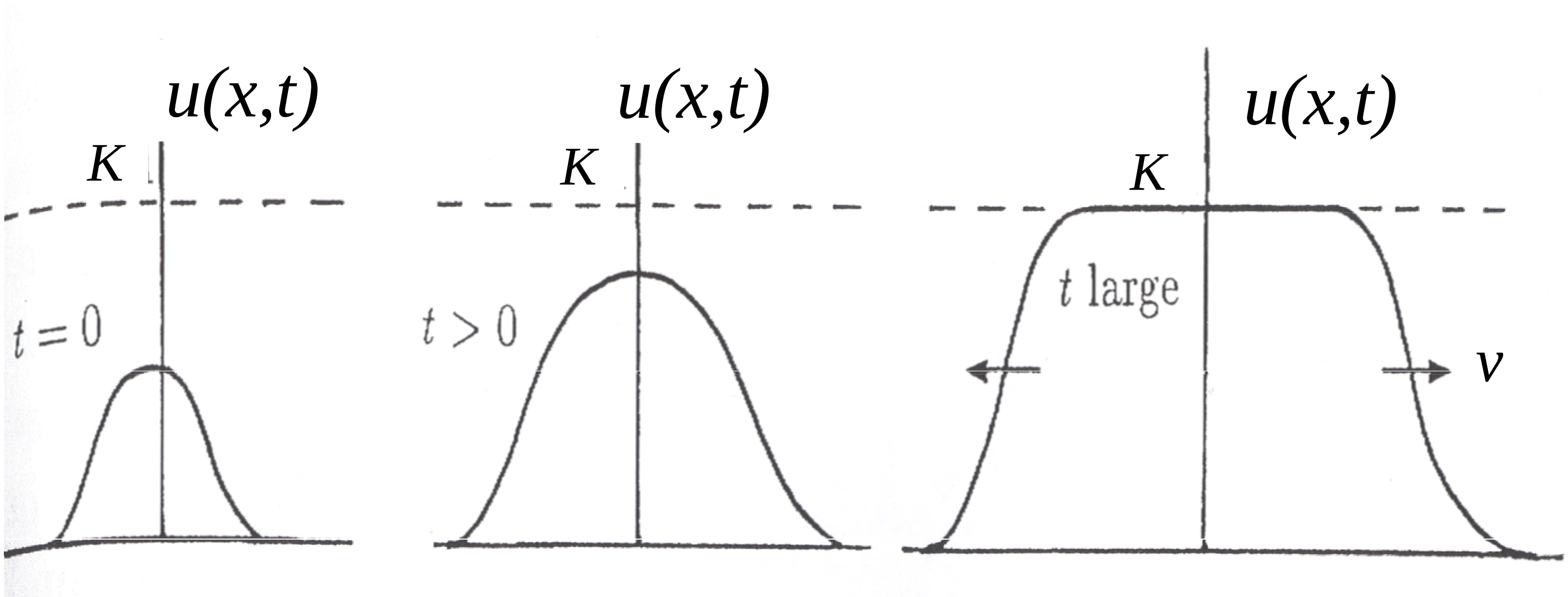
$D =$ effective viral diffusion constant in bacterial lawn

$a = a(k_1, k_{-1}, k_2, Y) =$ effective phage multiplication rate

What happens with this autocatlytic reaction-diffusion equation???

Fisher Wave of Plaque Growth In One Dimension

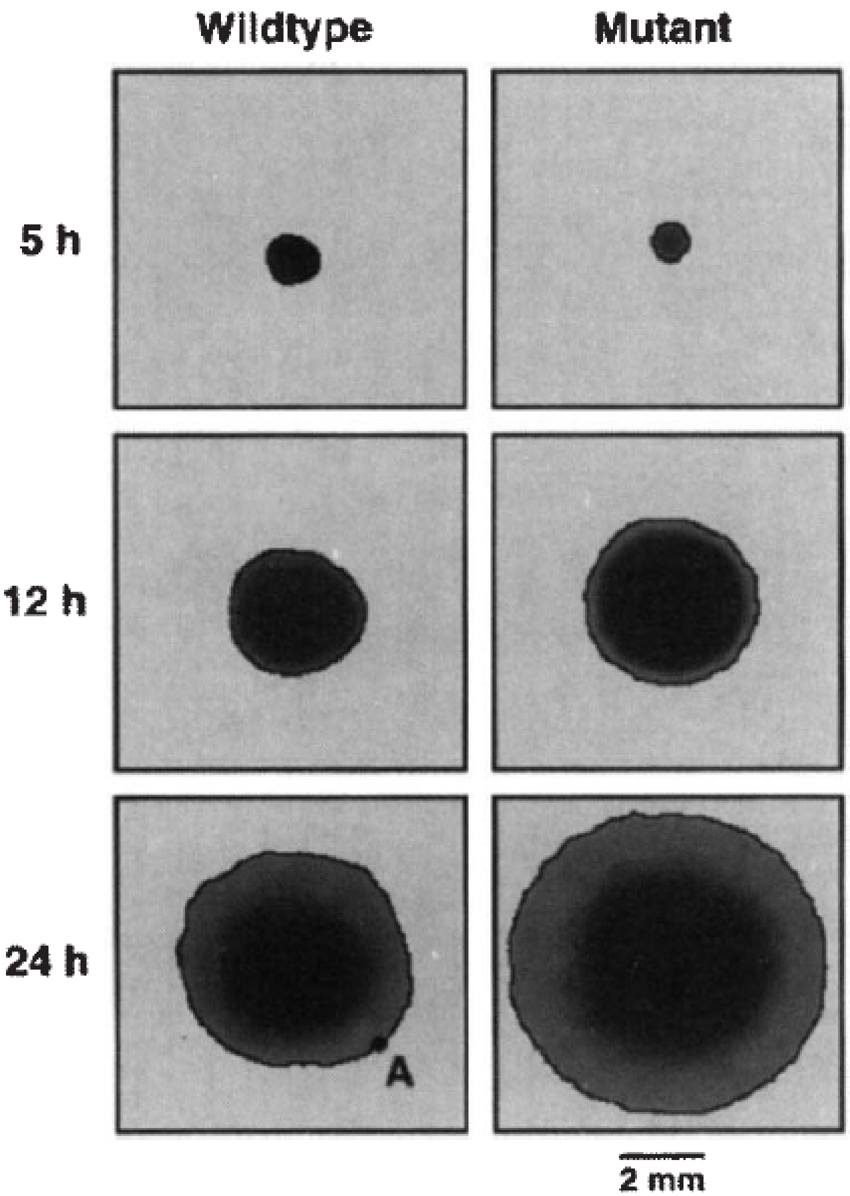
$$\frac{\partial}{\partial t}u(x,t) = D\frac{\partial^2}{\partial x^2}u(x,t) + au(x,t)[1-u(x,t)/K]; \quad let\ u(x,t) = f(x-vt)$$



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

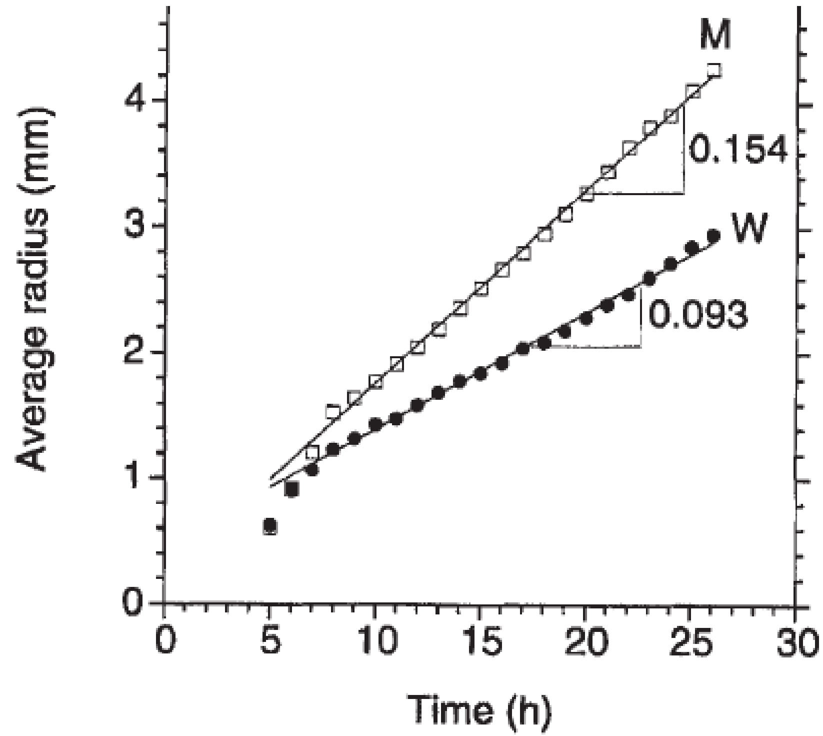
$Interface\ velocity\ v = 2\sqrt{Da}$ $\quad$ $Interface\ width = \sqrt{D/a}$

Front velocity of an T7 plaque invading a bacterial lawn



Mutant isolated from stab taken at point A of the wild type descendants

Y. Lee and J. Yin, Nat. Biotech. ***14,*** *491 (1996).*

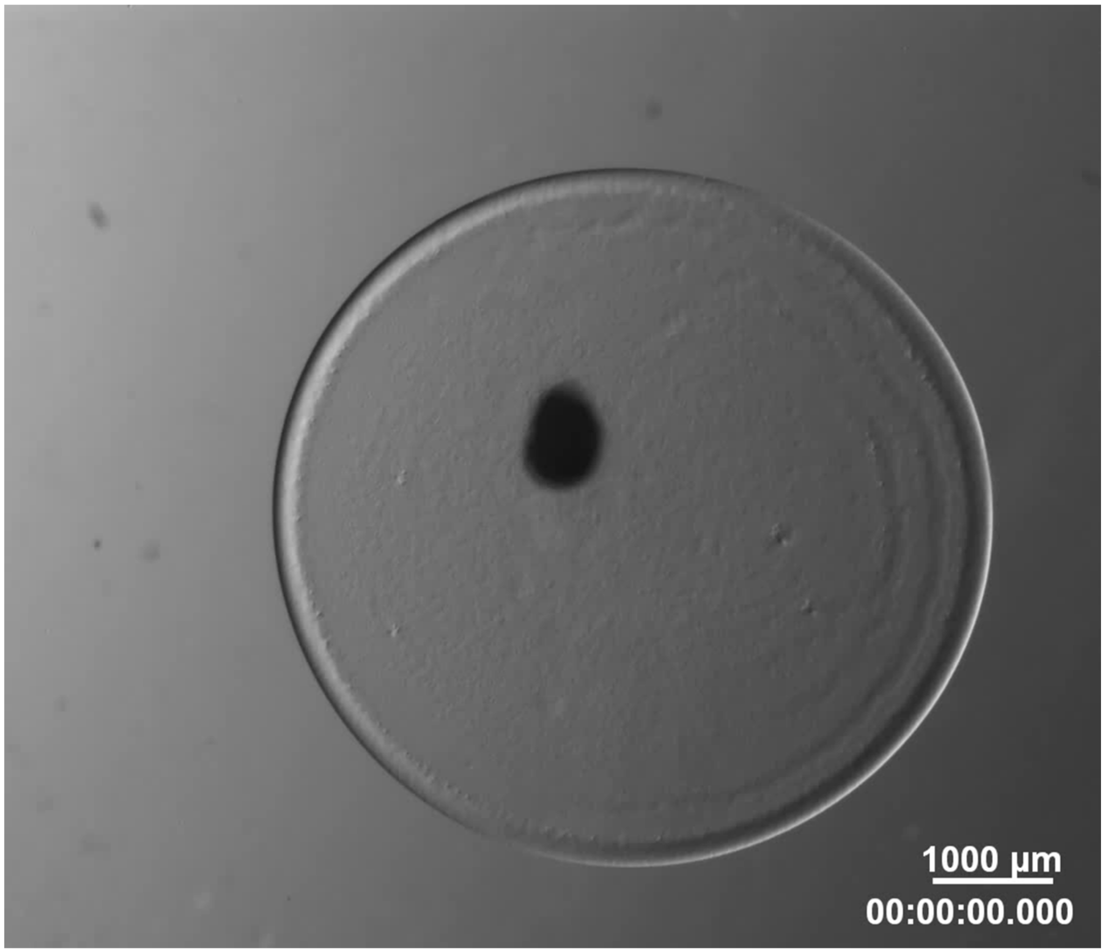


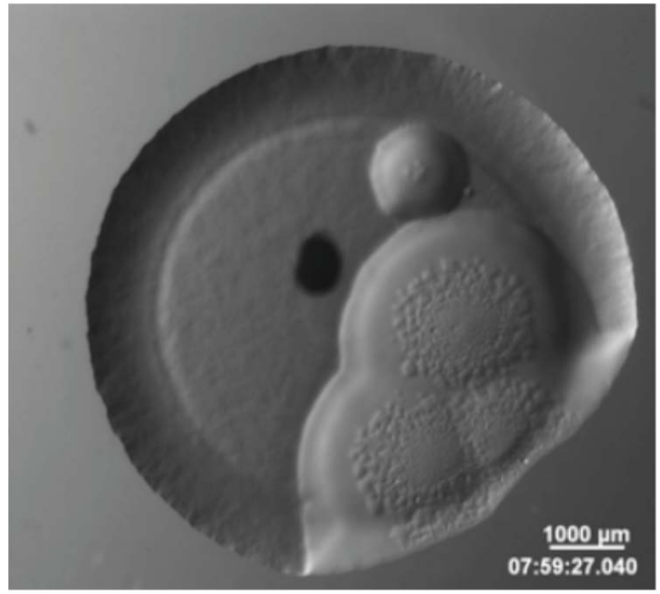
J. Yin and J. S. McCaskill, Biophys. J. ***61,*** *1540 (1992).*

$$V + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} I \xrightarrow{k_2} Y \cdot V$$

Infection resembles a Fisher population wave…

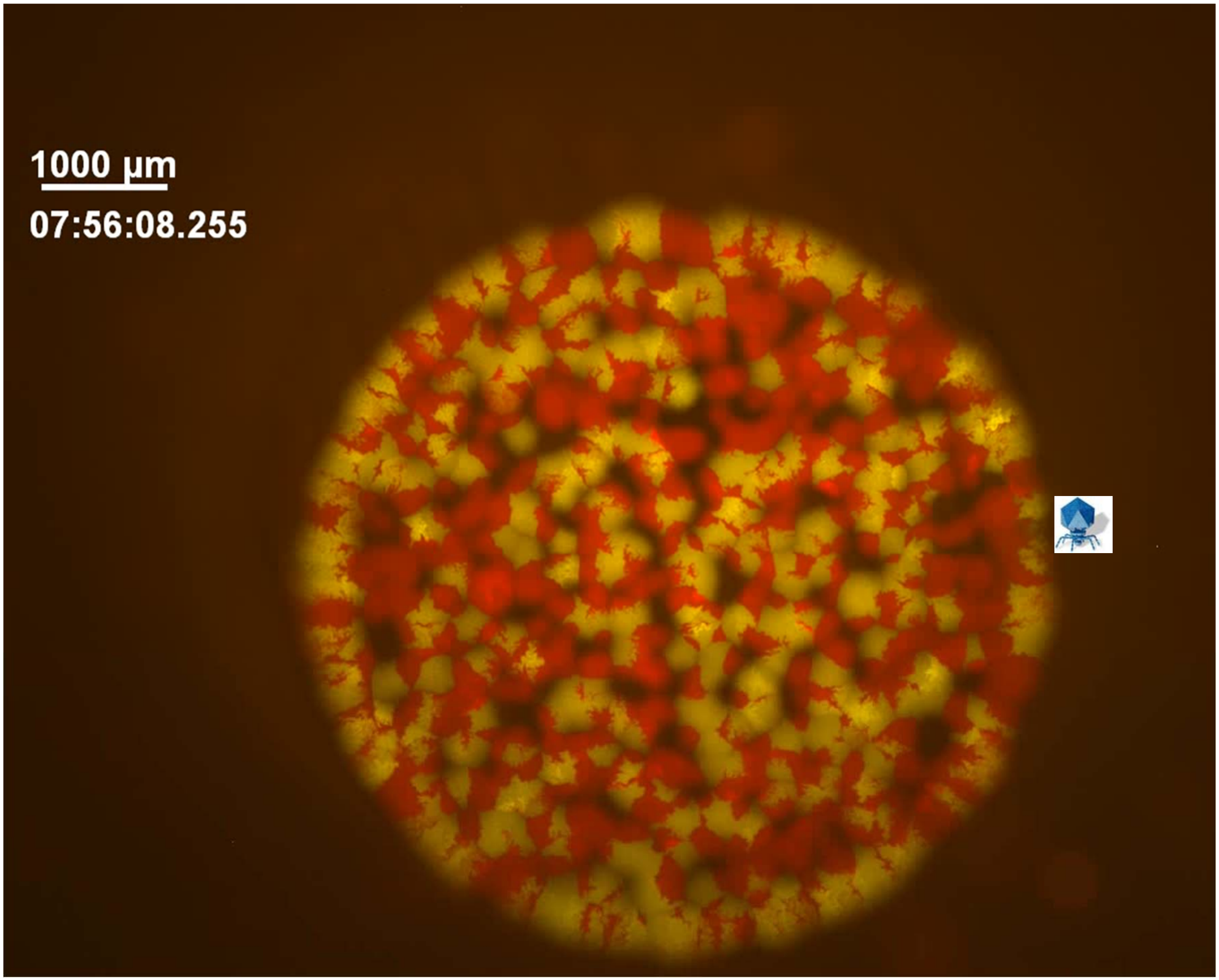
“Refraction” of a T7 population wave….



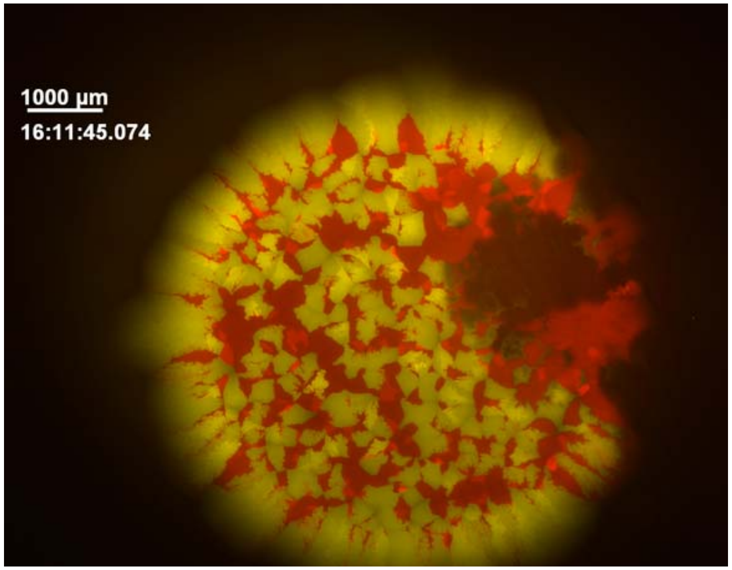


Spread of a T7 epidemic through the homeland

= T7-susceptible E. coli = T7-resistant E. coli



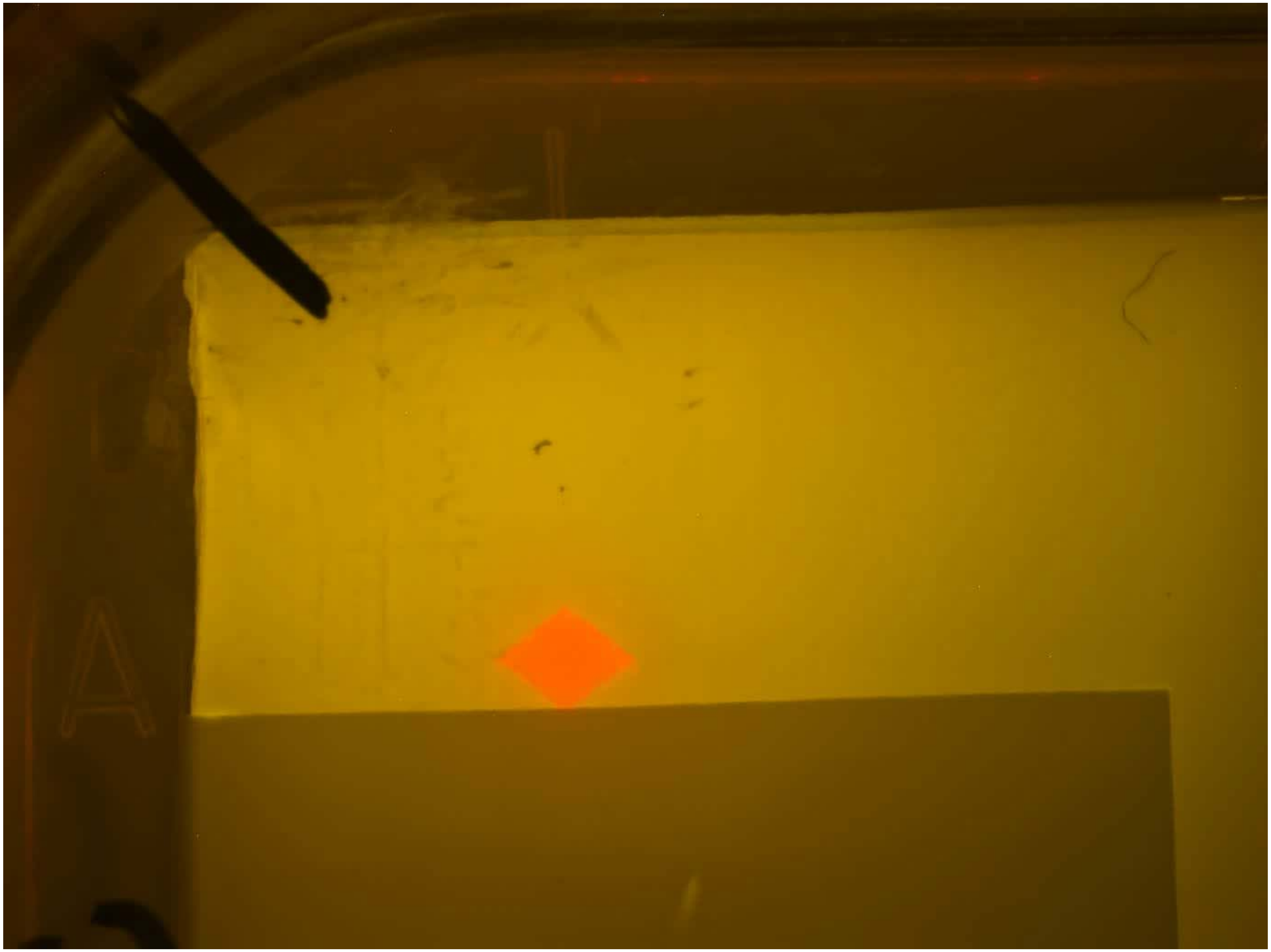
Simplify by focusing on a few well defined obstacles…



Wolfram's ink jet printer: (see also: Leibler Lab, PLoS 1, (2007)

Simplified problem: population dynamics around well-defined obstacles = "lakes"

plaque growth experiment



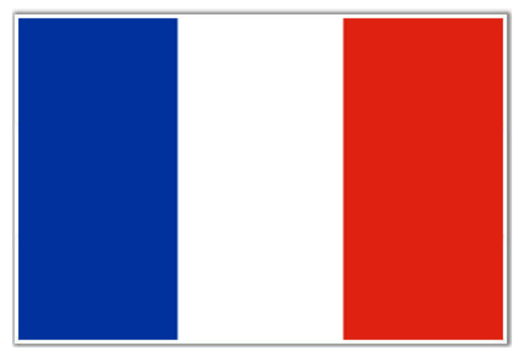
movie: 20120924

Christiaan Huygens (1629-1695)

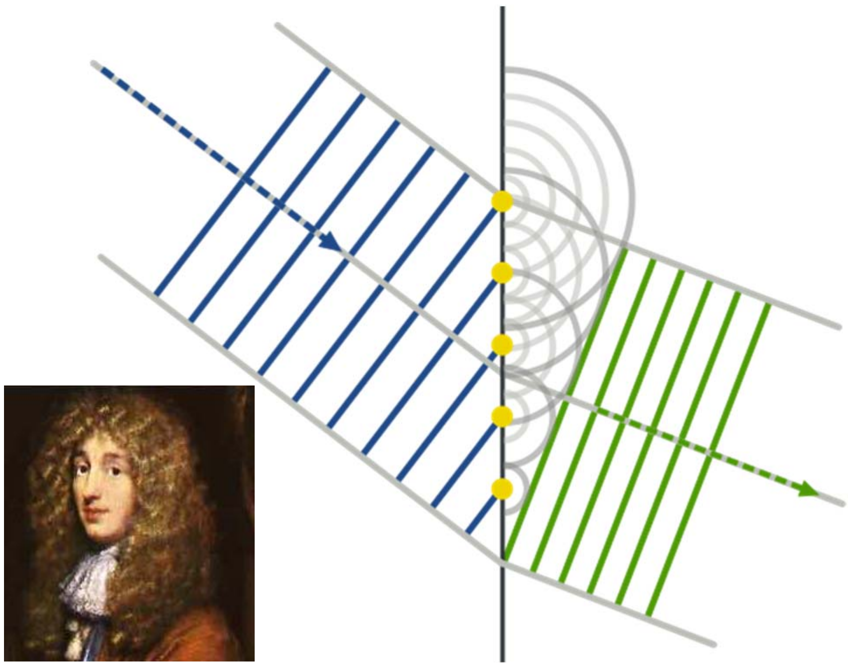
Dutch mathematician, physicist and astronomer who formulated the wave theory of light. (also, pendulum clock, centrifugal force, the rings of Saturn .

Pierre de Fermat (1601-1665)

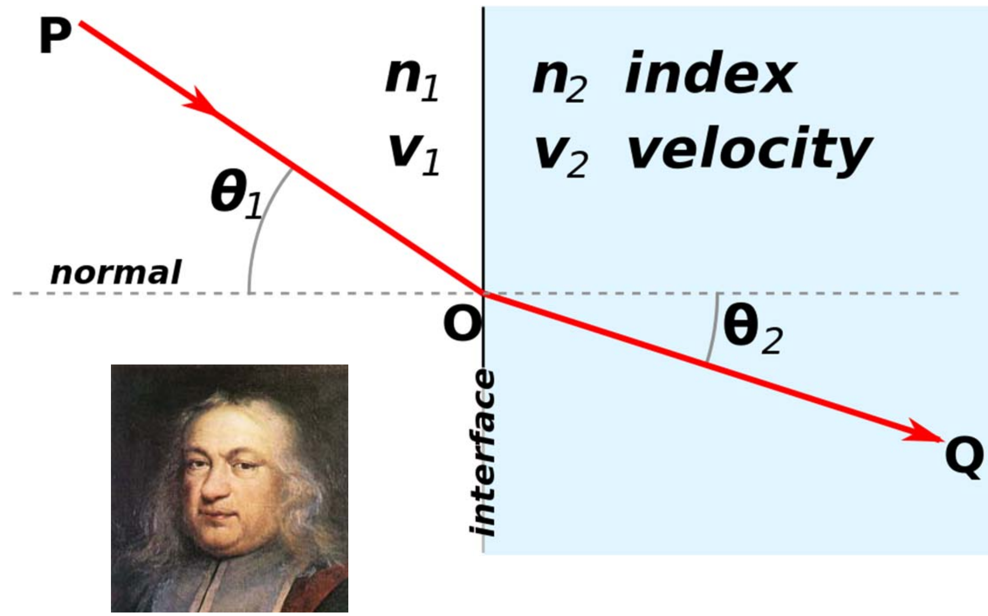
French lawyer at the Parlement of Toulouse, and amateur mathematician contributing to early developments leading to infinitesimal calculus.



Huygens' Principle



Fermat's Principle of Least Time



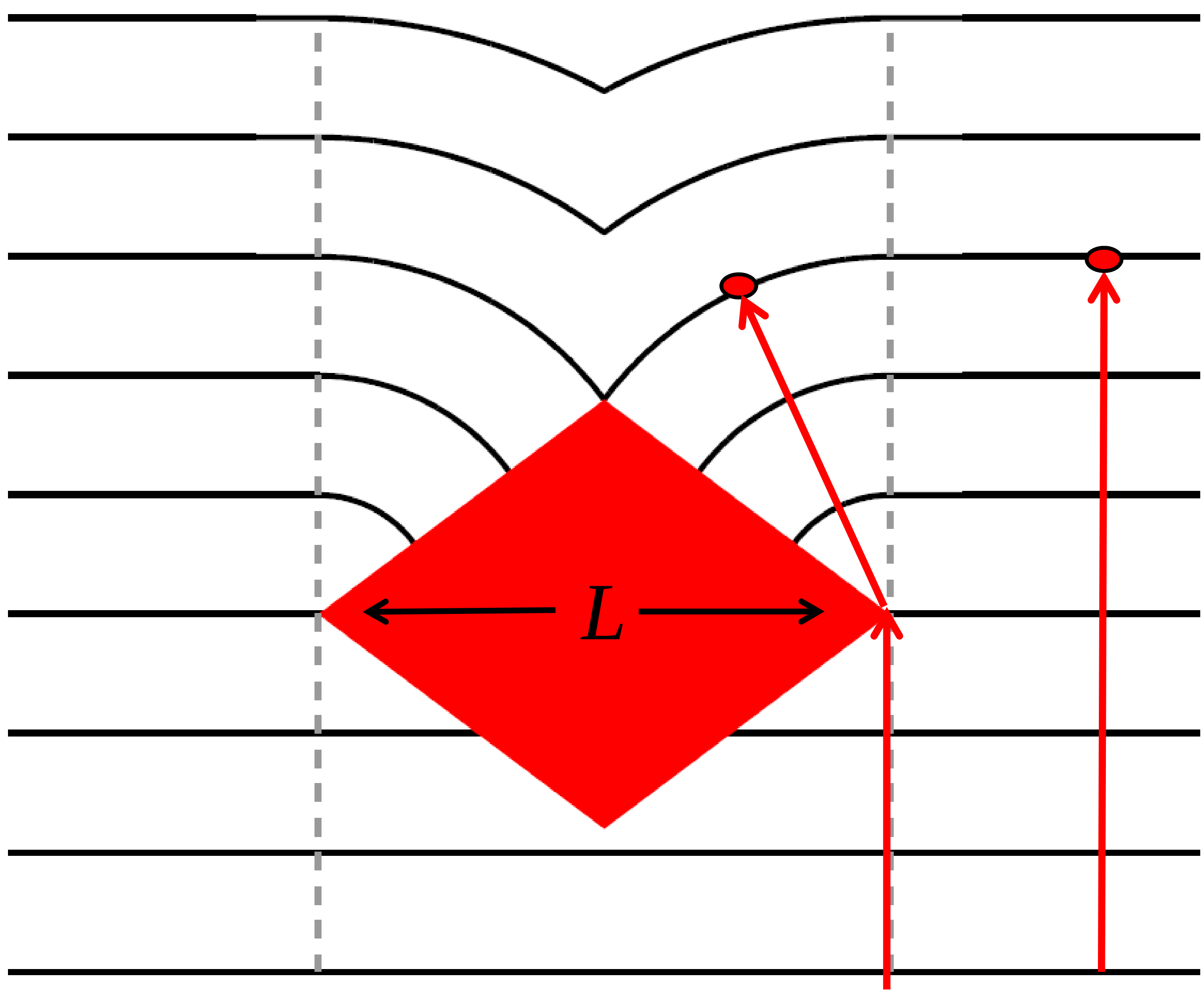
minimize over paths $\vec{r}(s)$, $s =$ arclength

$$T[\{\vec{r}(s)\}] = \int_A^B dt = \int_A^B \frac{dr(s)}{v[\vec{r}(s)]} = \int_A^B \frac{\vec{t}(s)}{v[\vec{r}(s)]} \cdot \frac{d\vec{r}(s)}{ds} ds,$$

$$\vec{t}(s) = \frac{d\vec{r}(s)}{ds} \quad \rightarrow \quad \frac{d}{ds}\left[\frac{1}{v[\vec{r}(s)]}\frac{d\vec{r}}{ds}\right] = 0$$

Fermat's principle for viral plaques *[require L >> sqrt(D_{eff}/a_{eff})]*

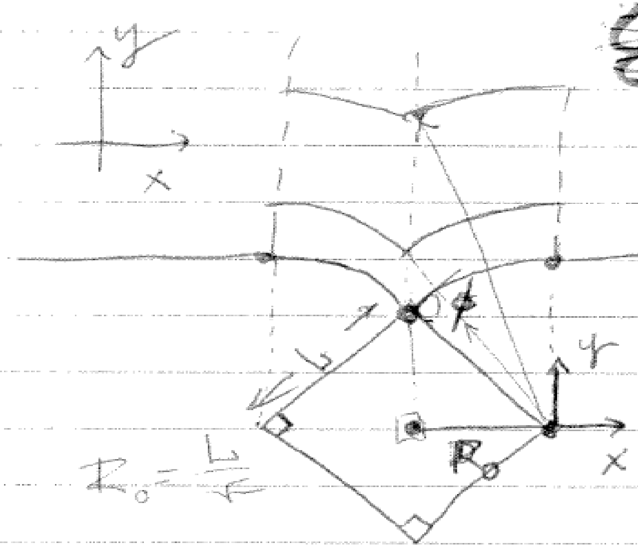
- ***At a given point on the frontier, ask "where did you ancestors come from?"***
- ***Resulting principle of least time equivalent to "survival of the fastest"***



ENVELOPEMENT OF OBSTACLES IN RANGE EXPANSIONS

1

DIAMOND-SHAPED OBSTACLE



$R_0 = \frac{L}{\sqrt{2}}$

$$(x-R_0)^2 + y^2 = (\sqrt{2}R_0 + vt)^2$$

$$2\,dx\,(x-R_0) + 2dy\,y = 0$$

$$\Rightarrow \frac{dy}{dx} = -\frac{(x-R_0)}{y} = \tan\phi$$

$$\tan\phi = \left.\frac{dy}{dx}\right|_{x=0} = \frac{R_0}{y}, \text{ but } y = \sqrt{(\sqrt{2}R_0+vt)^2 - R_0^2}$$

$$= \sqrt{R_0^2 + 2\sqrt{2}R_0 vt + v^2t^2}$$

$$\tan\phi = \frac{L/\sqrt{2}}{\sqrt{\frac{L^2}{2} + 2Lvt + v^2t^2}}$$

OR

$$\tan\phi = \frac{L}{\sqrt{L^2 + 4Lvt + 2v^2t^2}}$$

Thus as $t \to \infty$ $\quad \phi(t) \sim 1/2vt$

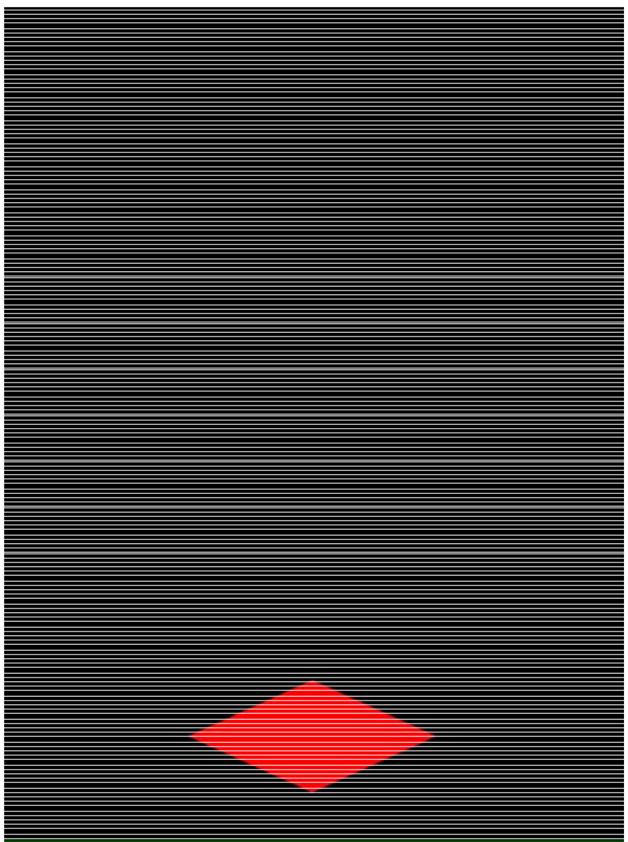
Simulations: T7 population dynamics around obstacles

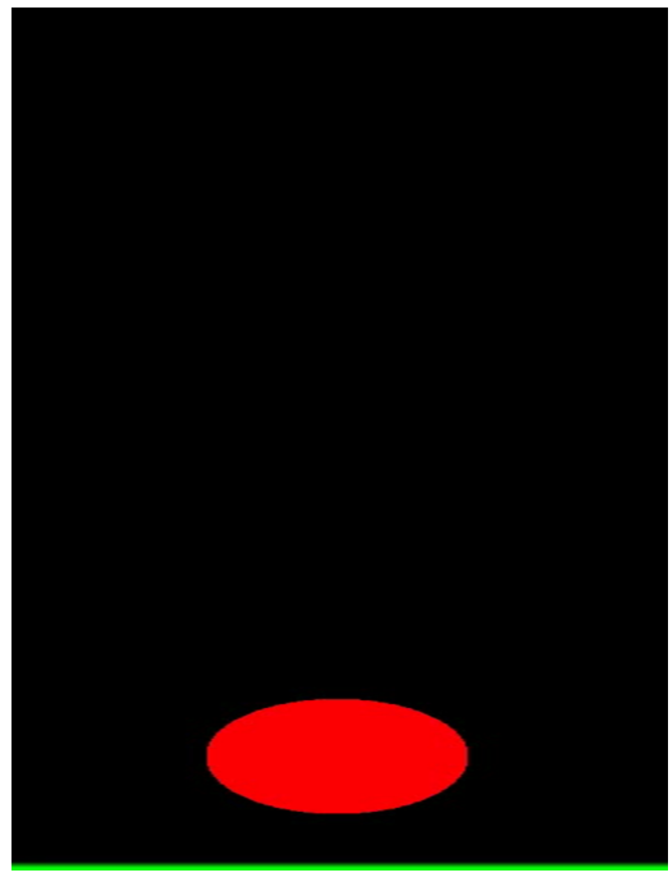
$$V + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} I \xrightarrow{k_2} Y \cdot V \quad (Y \sim 30)$$

$u(\vec{r},t) =$ phage density on plate

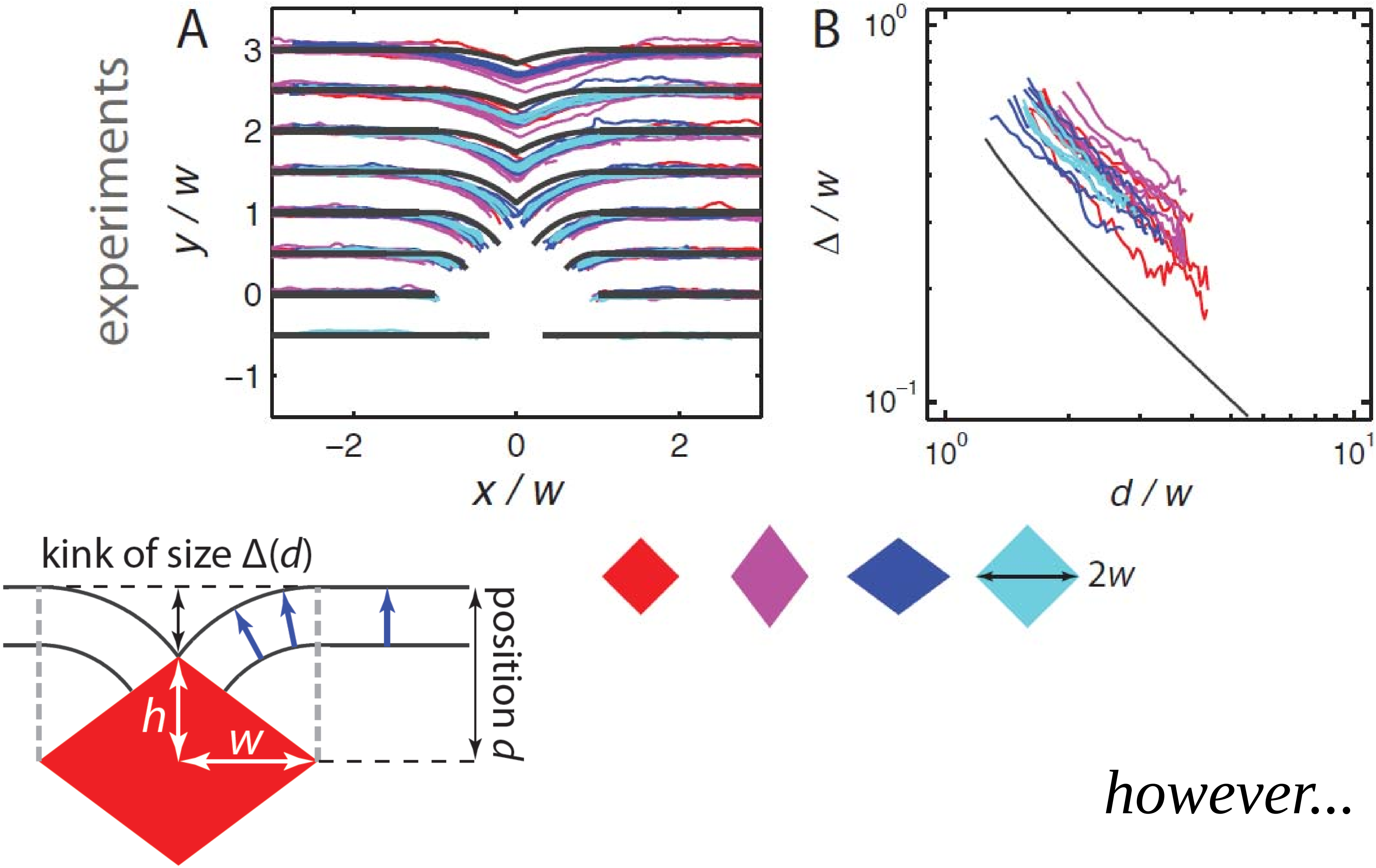
$$\frac{\partial u(\vec{r},t)}{\partial t} = D\nabla^2 u(\vec{r},t) + a(\vec{r})u(\vec{r},t)[1 - u(\vec{r},t)/K]$$

$a(\vec{r}) = 0$ inside obstacles



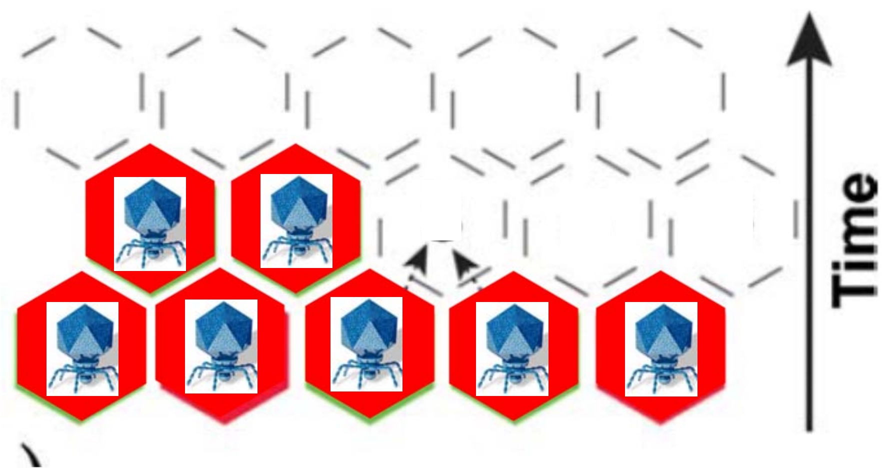


Cusps heal according to $\Delta \sim 1/d$, independent of the width of the obstacle

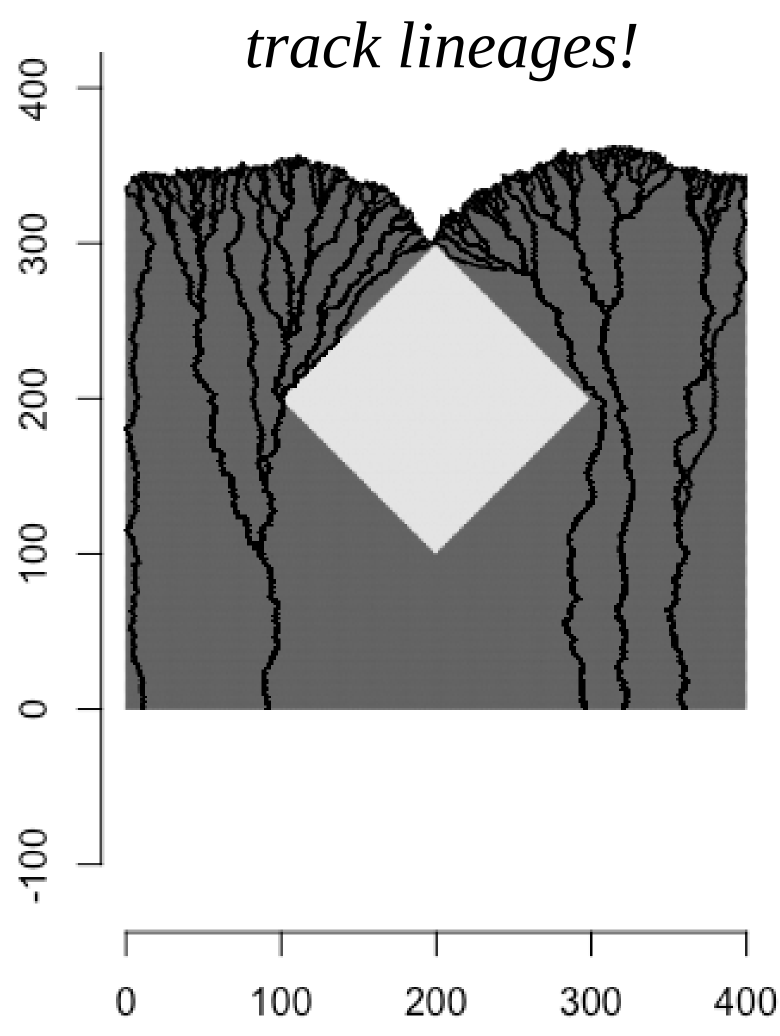


however...

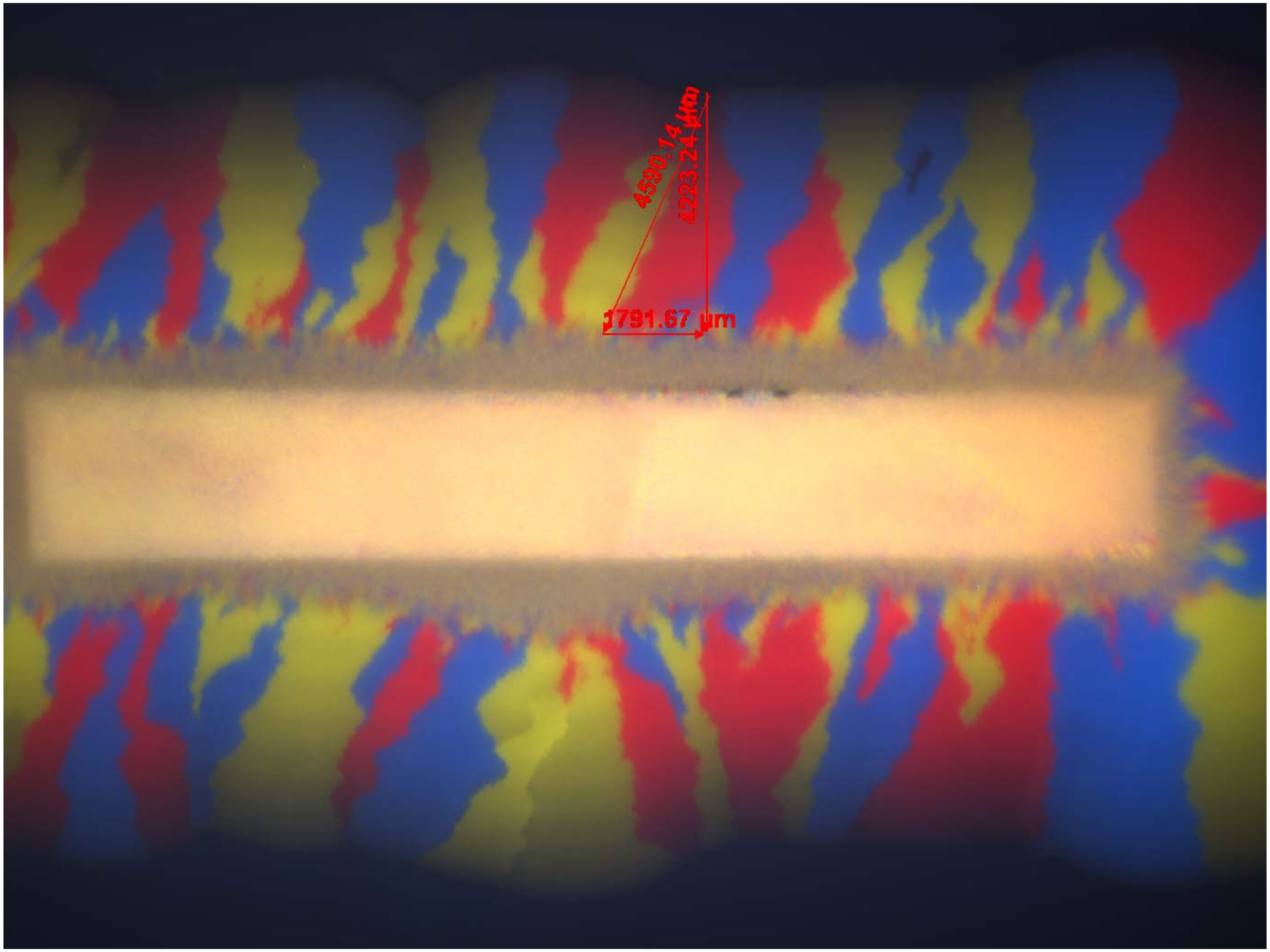
Huygens-Fermat principle neglects discreteness of viruses and cells...



It's only a good first approximation, like ray optics, which neglects photons and the wave nature of light!



Population genetics and range expansions (note genetic drift!)



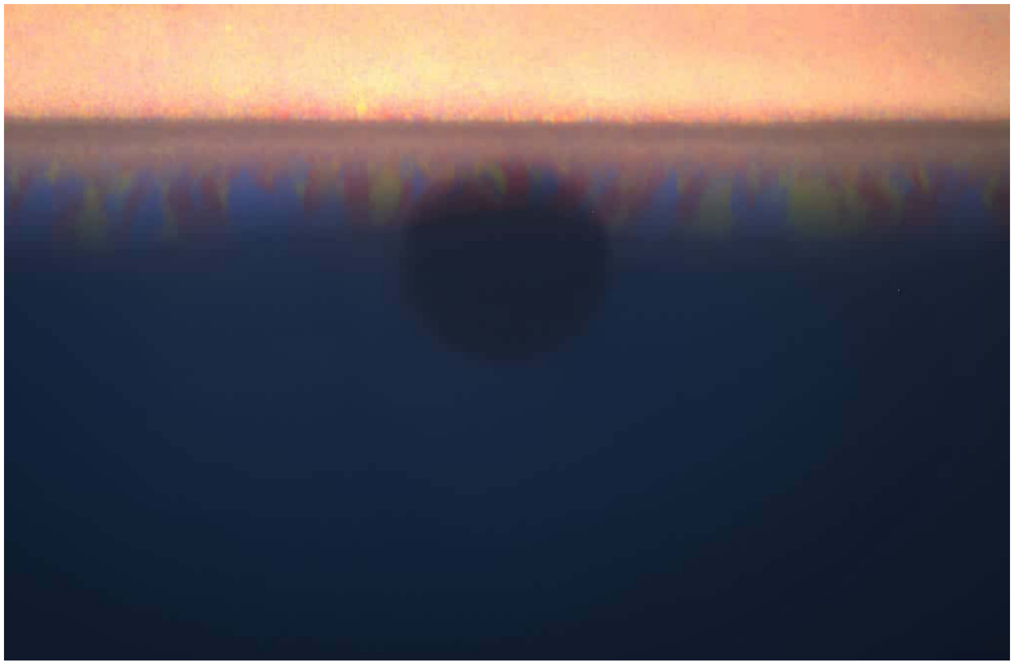
Wandering of genetic boundaries during range expansions given by a "wall diffusion constant".

$D_w \approx a^2/\tau_g$
a = cell size
τ_g ***= division time***

What happens if we add an obstacle????

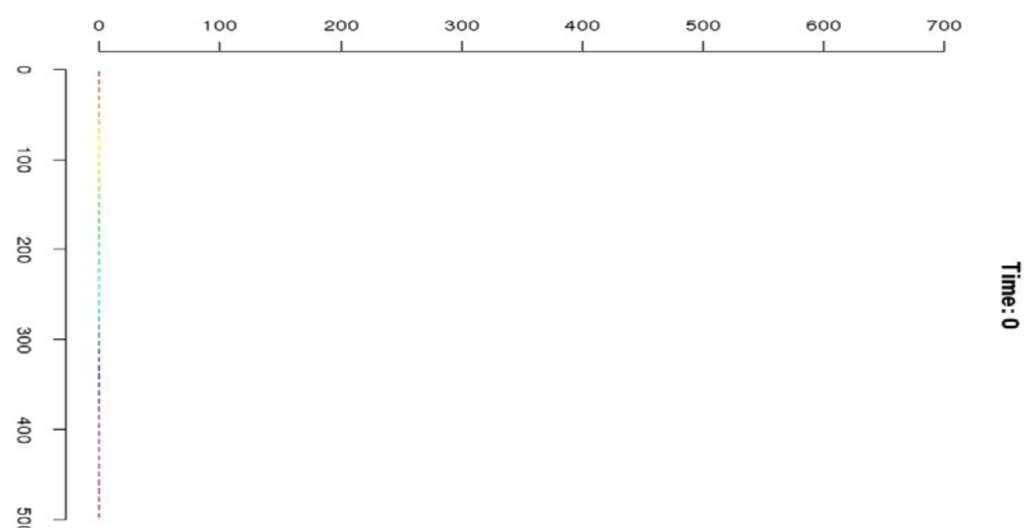
Population genetics near obstacles:

E. coli colonies obstructed by a disk impermeable to nutrients



Simulation of an
"infinite color" model

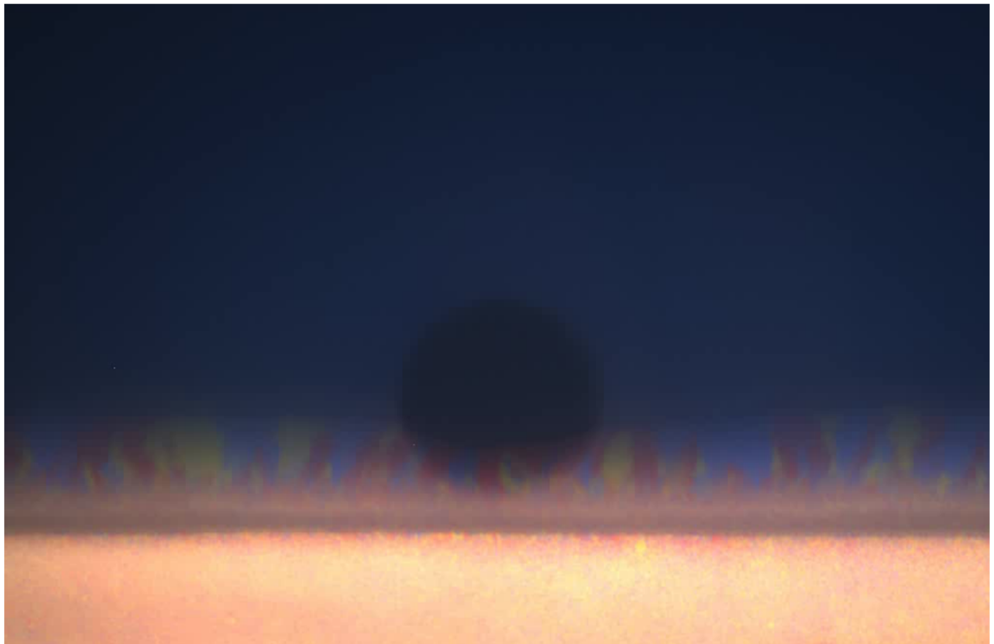
"selection by geometry"

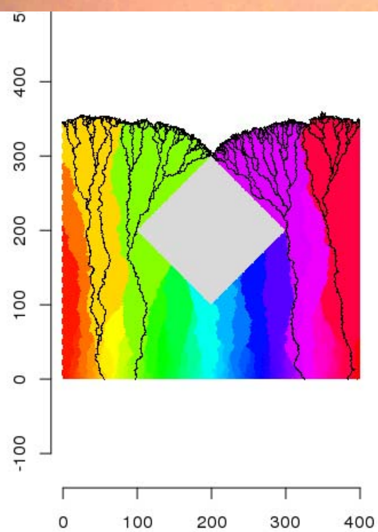


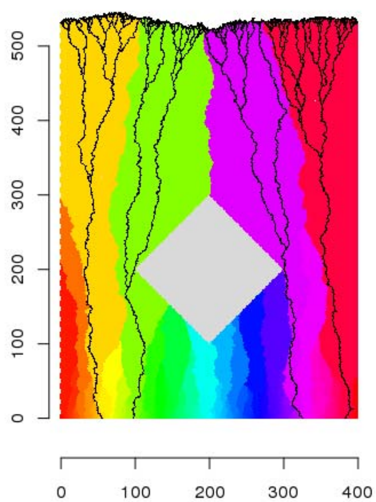
13etc

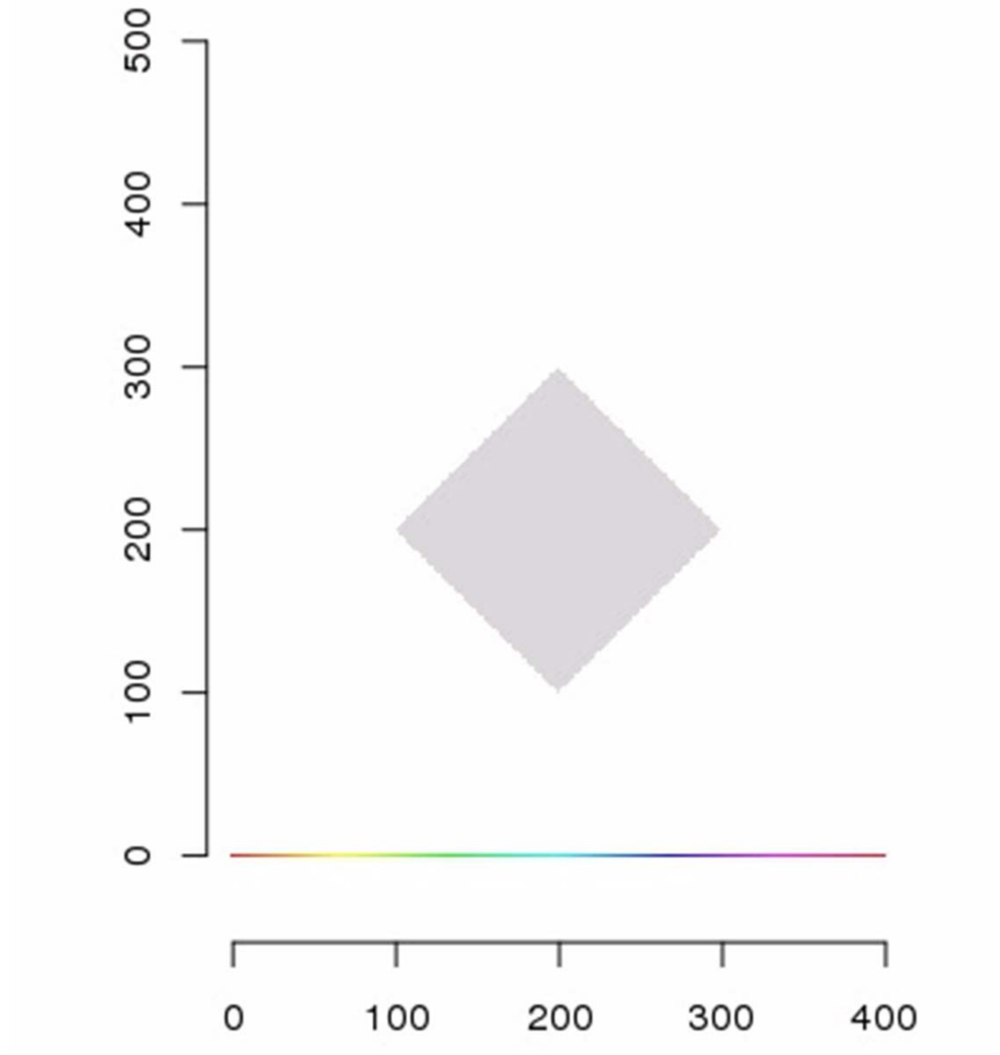
Coalescent lineages for range expansions around a "lake"

(Wolfram Moebius …)







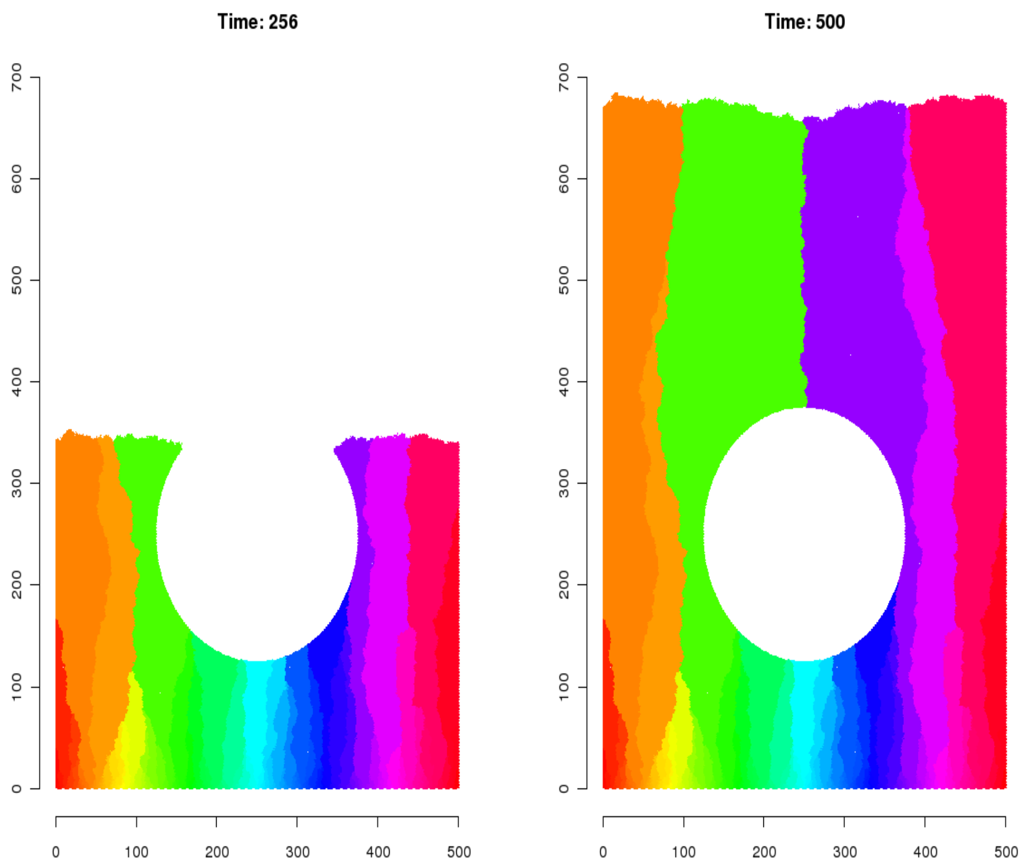


simulation ↔ Huygens principle ↔ bacterial growth experiment

Population genetics of fronts impinging on obstacles

- *Obstacles impress long-lived characteristic footprints on allele frequency patterns at population frontiers.*

- *Populations migrating through inhomogenous media above the percolation threshold will be described by an index of refraction*



- obstacles reduce genetic diversity ('unlucky genotypes')
- obstacles putatively boost genotypes ('lucky genotypes')
- cusps behind obstacles eventually heal, but sector boundaries caused by obstacles can persist indefinitely
- "Selection by Geometry"

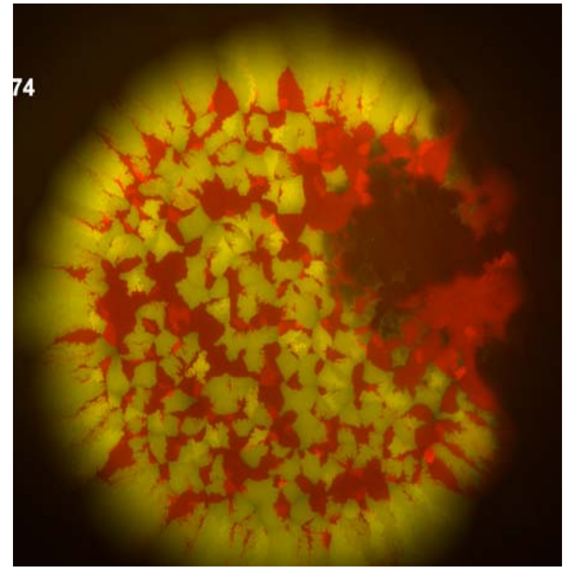
Genetically structured vs. spatially structured populations

T7 "out of Africa": can print bacterial lawns for T7 in arbitrary patterns…. Wolfram Moebius, unpublished

= T7-susceptible E. coli   = T7-resistant E. coli

Wolfram Moebius

Range Expansions in Structured Environments



Frontier population genetics with spatial structure

--Range expansions are very common in biology… Number fluctuations very large at the edge of a population wave

-- our world is not a sphere of agar → geographical features influence ecosystems and range expansions

→ How does a range expansion in a non-homogeneous environment shape genetic diversity?

Wolfram Moebius
Andrew Murray

Simplified model of spatial structure: migration around a "lake"

-- population fronts around obstacles: simulations, experiments, and geometrical arguments

---adding population genetics: simulation and an experiment with E. coli

Wolfram

Andrew

Genetically structured vs. spatially structured populations

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