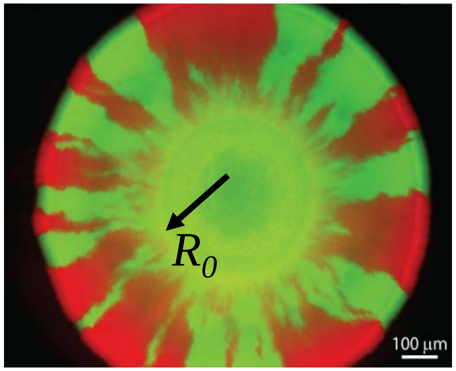
The Physics of Life:
Spatial Population Genetics

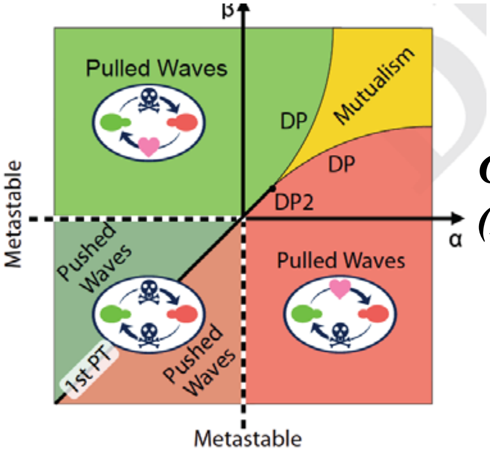
I. Introduction to spatial population genetics

II. Pushed genetic waves and antagonistic interactions

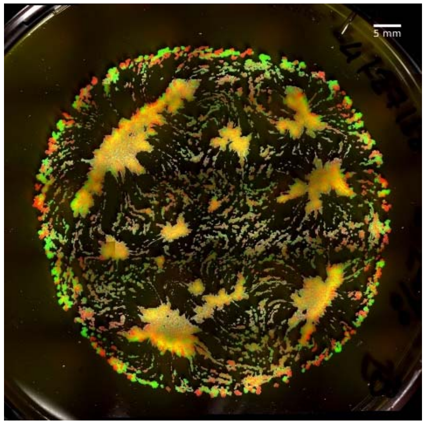
III. Microbial interactions and expansions on liquid substrates



P. Aeruginosa
(J. Xavier et al.)



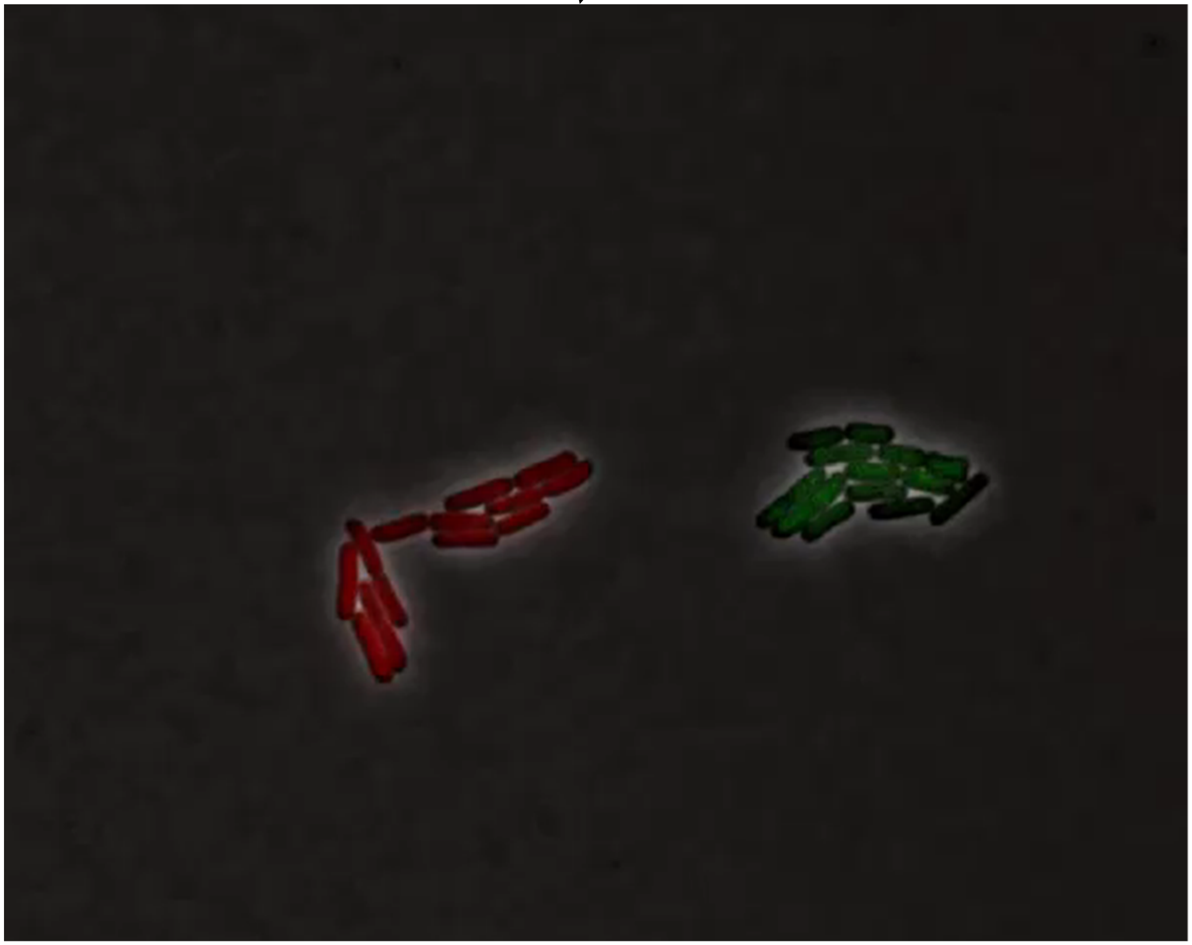
Game theory:
(E. Frey et al.)



S. cerevisea
(S. Atis et al.)

"Clash of Genomes": Range expansions with neutrality, selection advantage, cooperation or competition

What happens at the border?

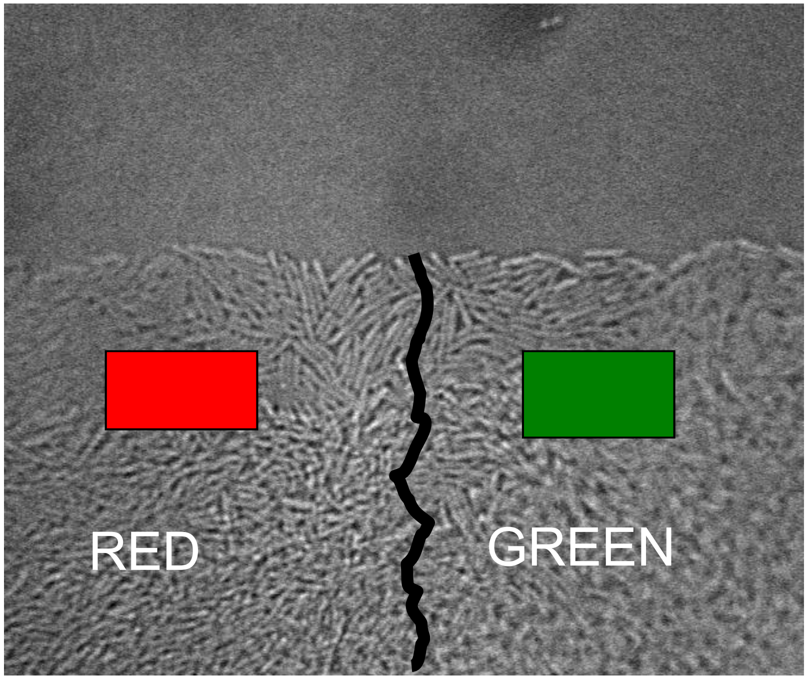


Collision of two neutral genetically labelled E. Coli colonies on hard agar….

Hernan Garcia,
Rob Phillips & drn

Range Expansions with Competition or Cooperation

***Recall*:**



See Populus program…

In 500 generations….

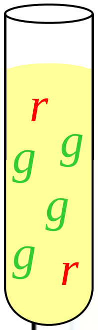
Large mammals expand over ~10^4 km

Bacteria (in a Petri dish) expand ~ 1 cm

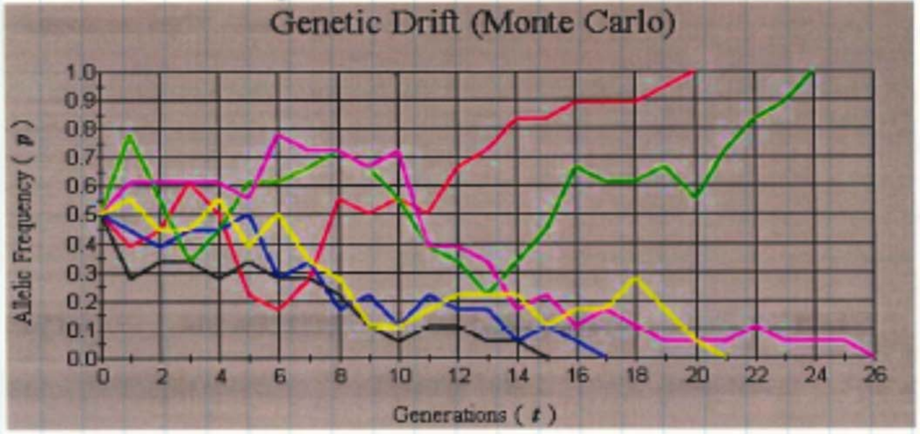
Red and Green Strains….

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

Genetic drift in well-mixed neutral models



DIPLOID
Population Size: $N = 10$



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

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

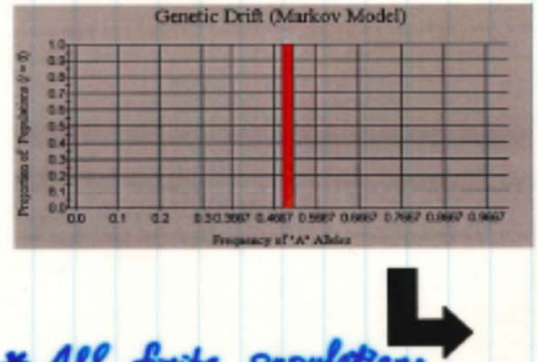
M. Kimura, Genetics 47, 713 (1962)

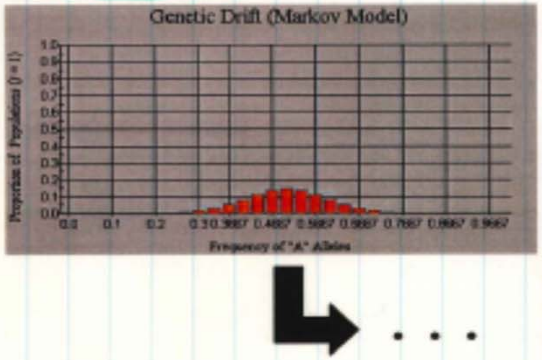
i random walk dynamics of gene frequencies!

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

- Finite populations go to fixation for long times ...

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





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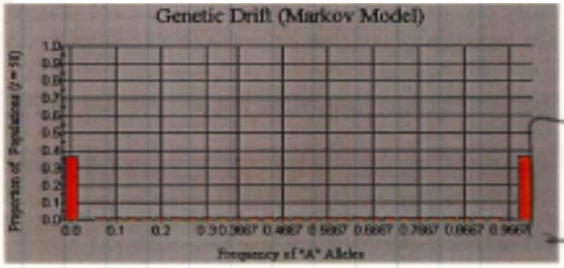
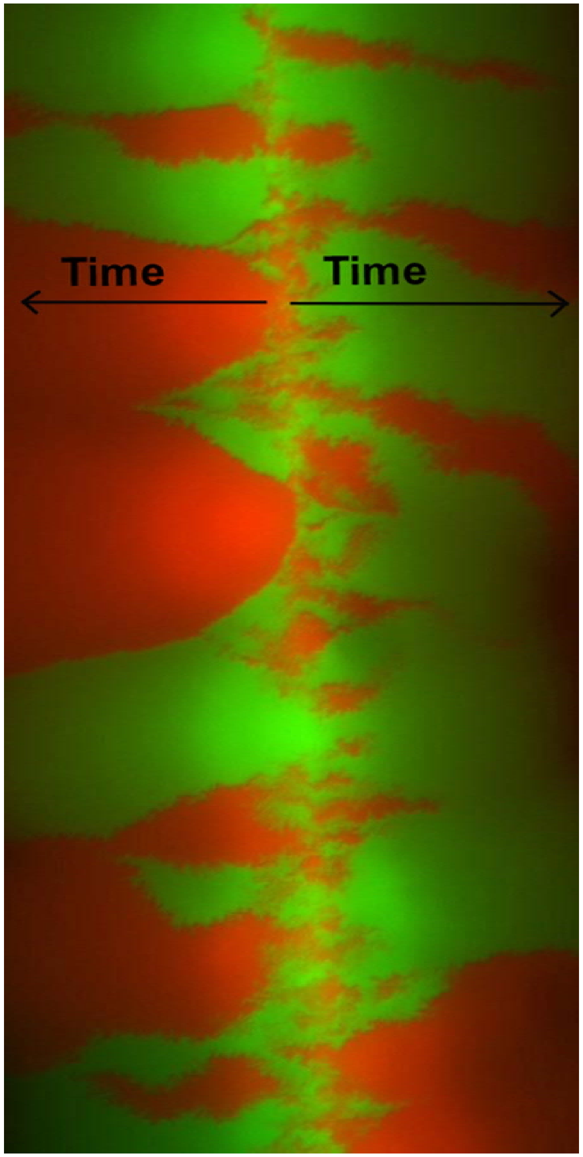
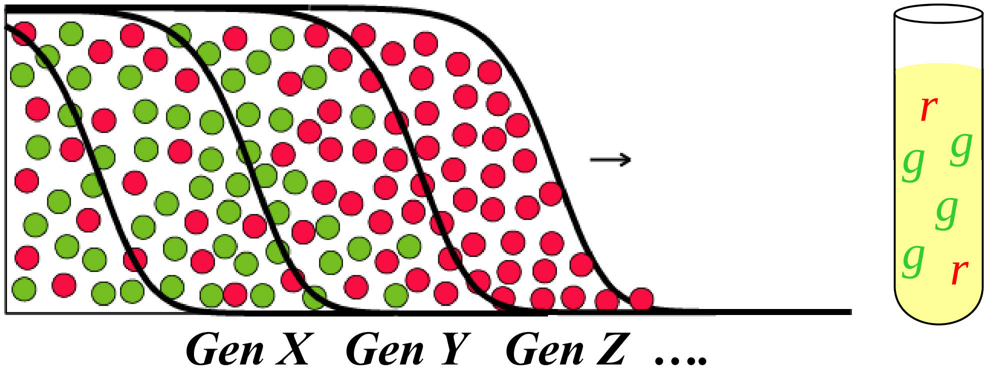


* All finite populations eventually fixed with homozygous population of all (a/a) or all (A/A)

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





- In effect, a moving population front is a serial dilution experiment in a well mixed test tube

How do we add a selective advantage?

go to board 1

Selective Advantage

assume $W_G > W_R$ so green as a selective advantage

* Let W_G = # of **green** offspring in each time step
W_R = # " **red** " " " " "

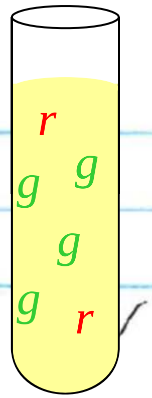
$f_G(t)$ = green fraction
$1 - f_G(t)$ = red fraction

$$f_G(t+\tau_g) - f_G(t) = \frac{W_G f_G}{W_G f_G + W_R(1-f_G)} - f_G = \frac{(W_G - W_R) f_G (1 - f_G)}{\frac{1}{2}(W_G + W_R) + \frac{1}{2}(W_G - W_R)(2f_G - 1)}$$

* assume W

* If $|W_G - W_R| \ll \frac{1}{2}(W_G + W_R)$ (small selective advantage), then

$$\boxed{\frac{df_G}{dt} \approx s f_G (1 - f_G), \quad s = \frac{2(W_G - W_R)}{\tau_g (W_G + W_R)}}$$

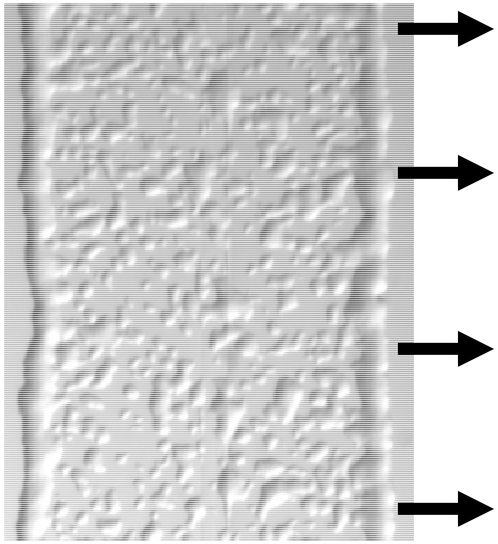


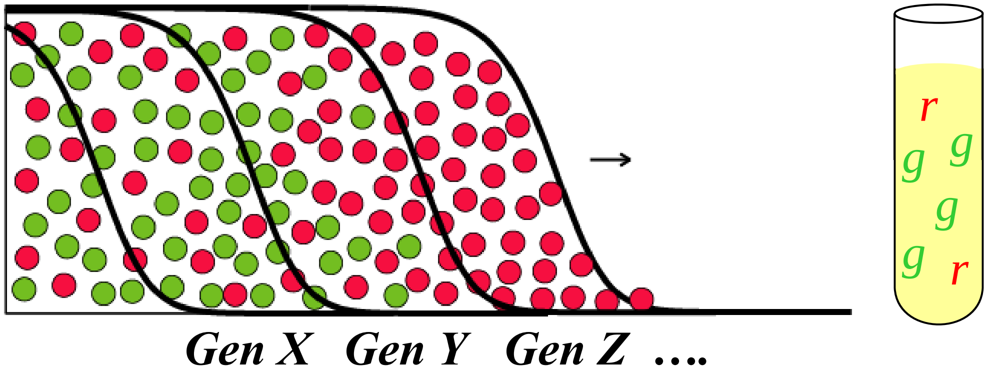
$$f_G(t) = \frac{f_G(0)e^{st}}{1 + f_G(0)(e^{st} - 1)}$$

FKPP equation for a *genetic* wave

$$\frac{\partial f_G(x,t)}{\partial t} = D\frac{\partial^2 f_G}{\partial x^2} + s f_G (1 - f_G)$$

Genetic Drift & Selection





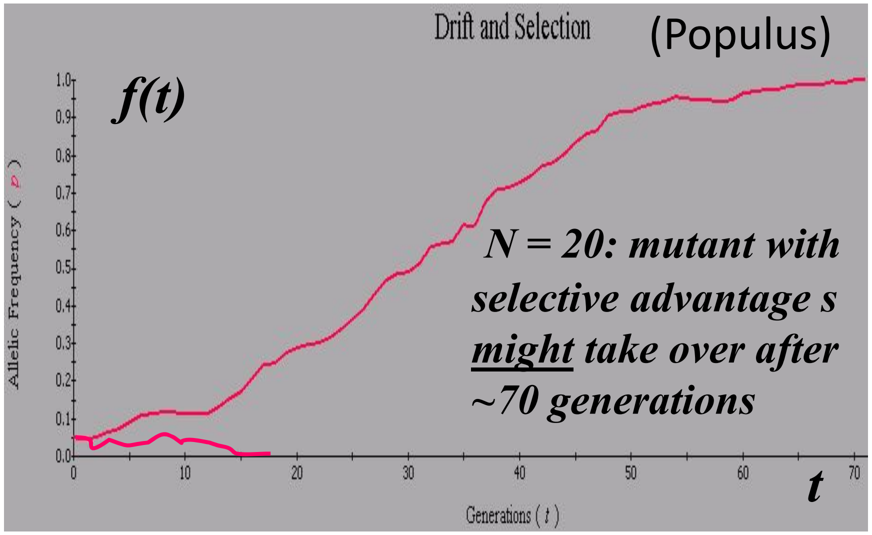
➲In effect, a moving population front is a serial dilution experiment in a well mixed test tube

For a “zero-dimensional” frontier, *f(t)*, the fraction of red cells with selective advantage s at time *t obeys*

$$\frac{df(t)}{dt} = sf(1-f) + \sqrt{\frac{f(1-f)}{2N}}\,\Gamma(t)$$

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

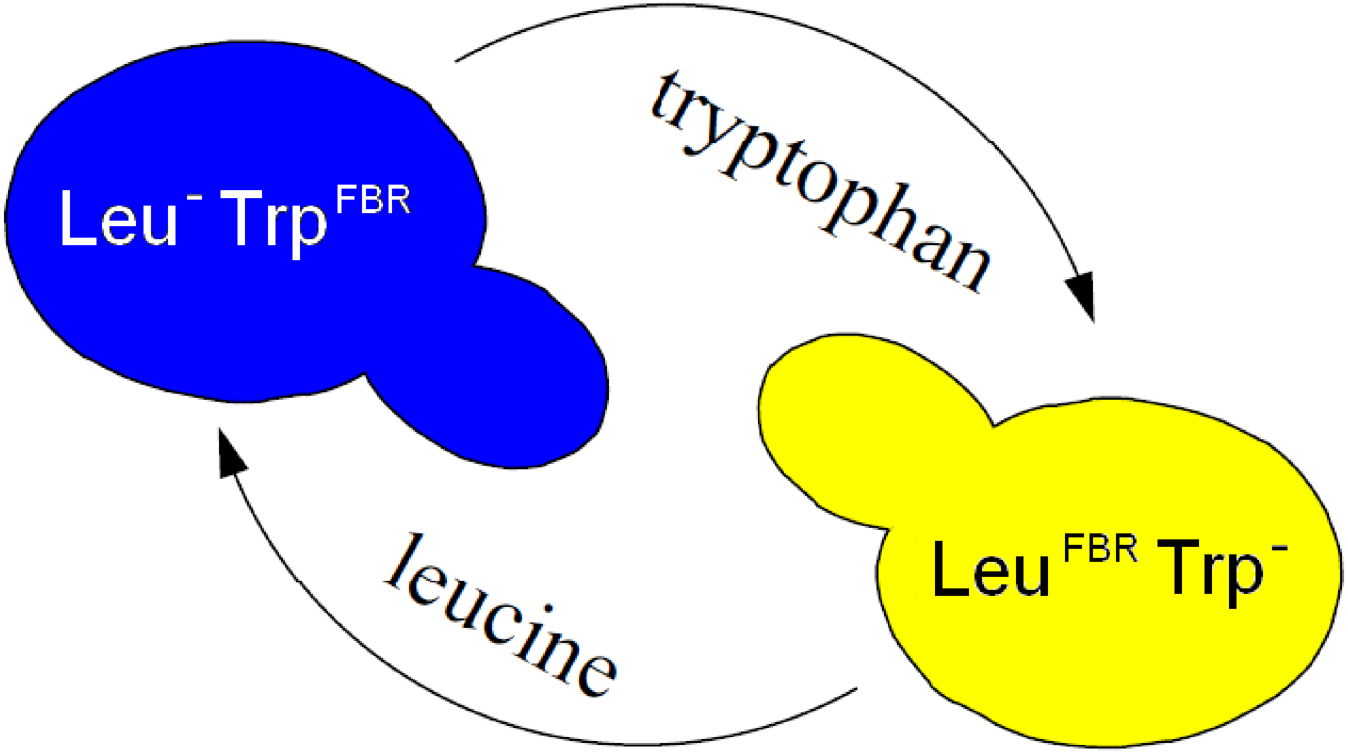
$$s = 2\frac{w_R - w_G}{w_R + w_G}$$



N = 20: mutant with selective advantage s might take over after ~70 generations

Range expansions for <u>mutualists</u>

M. Mueller, A. Murray K. Korolev & drn



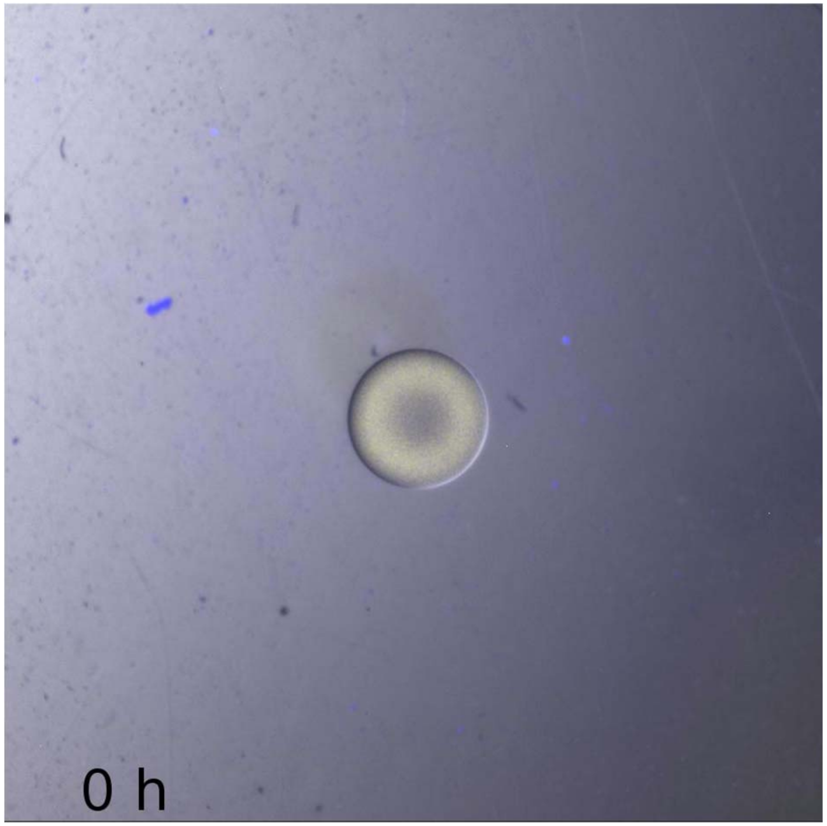
FBR = "feed back resistant"

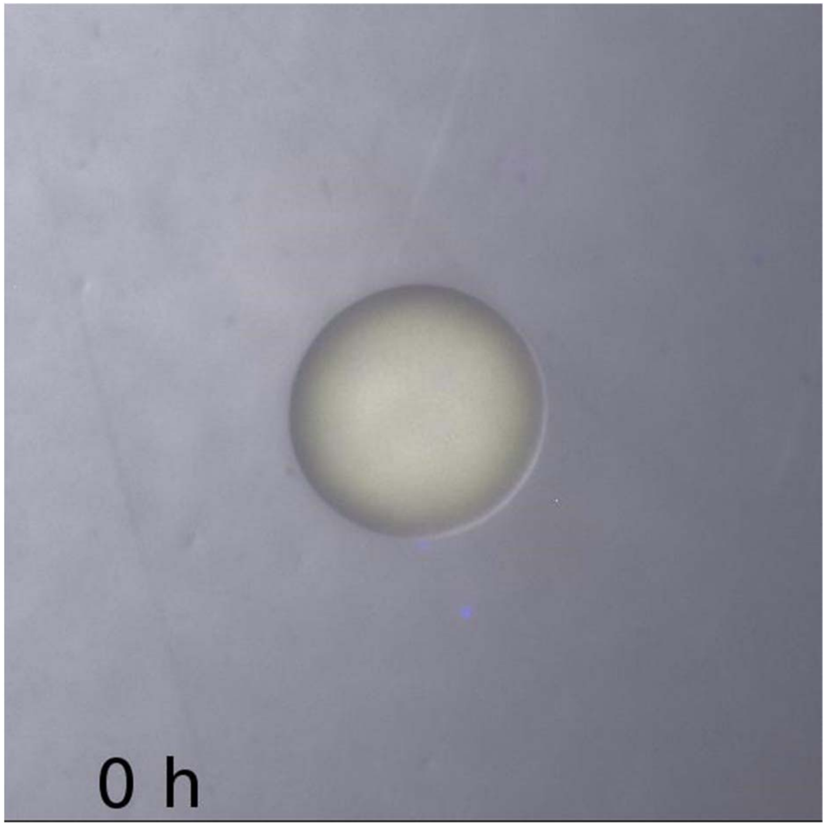
Mutualism: *survival requires exchanging amino acids, if leucine and tryptophan are not already present in the natural environment*

Mutualists on various substrates (Mueller, Murray, drn)

CSM (abundant Leu & Trp)
→ Mutualism unimportant

CSM-Leu-Trp (Leu, Trp missing)
→ Obligate mutualism





go to board 3

Game Theory and Frequency-Dependent Selection

If w_B and w_Y are the number of blue and yellow offspring produced during one generation at a given point on the frontier...

selective advantage $s \approx 2\dfrac{w_B - w_Y}{w_B + w_Y}$

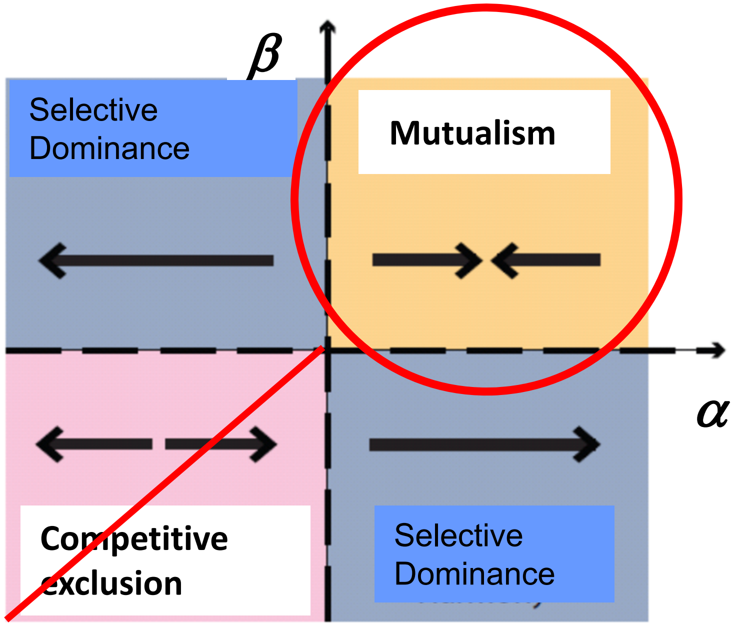
If $f(x,t)$ is the yellow fraction, describe mutualism by...

$$w_Y(x,t) = g + \beta(1 - f(x,t))$$
$$w_B(x,t) = g + \alpha f(x,t)$$

$$s(f) \approx s_0(f^* - f)$$
$$s_0 = (\alpha + \beta)/g$$
$$f^* = \beta/(\alpha + \beta)$$

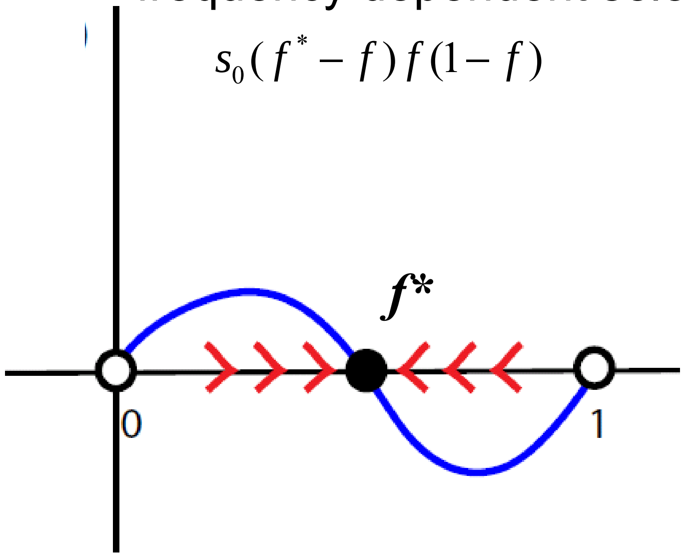
$$\frac{\partial f(x,t)}{\partial t} = D\frac{\partial^2 f(x,t)}{\partial x^2} + s_0(f^* - f)f(1 - f)$$

$\alpha, \beta > 0 \rightarrow$ Mutualism

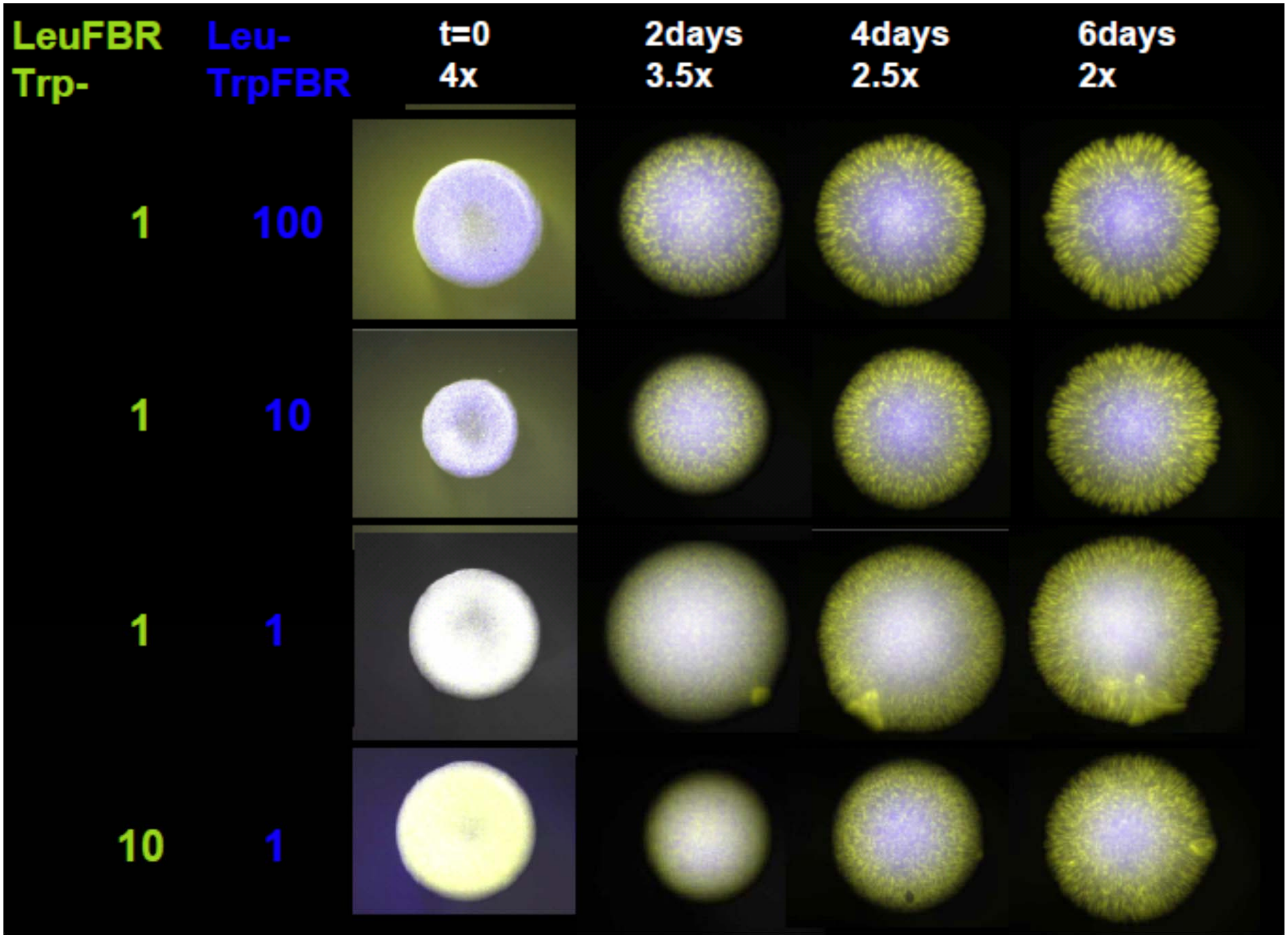


M. Nowak et al., Nature (2004)
J. Gore et al. Nature (2009)
E. Frey et al., Phys. Rev. Lett. (2010)

frequency dependent selection:


$s_0(f^* - f)f(1 - f)$

Experiments reveal that an "evolutionary stable strategy" is indeed reached independent of the initial condition…



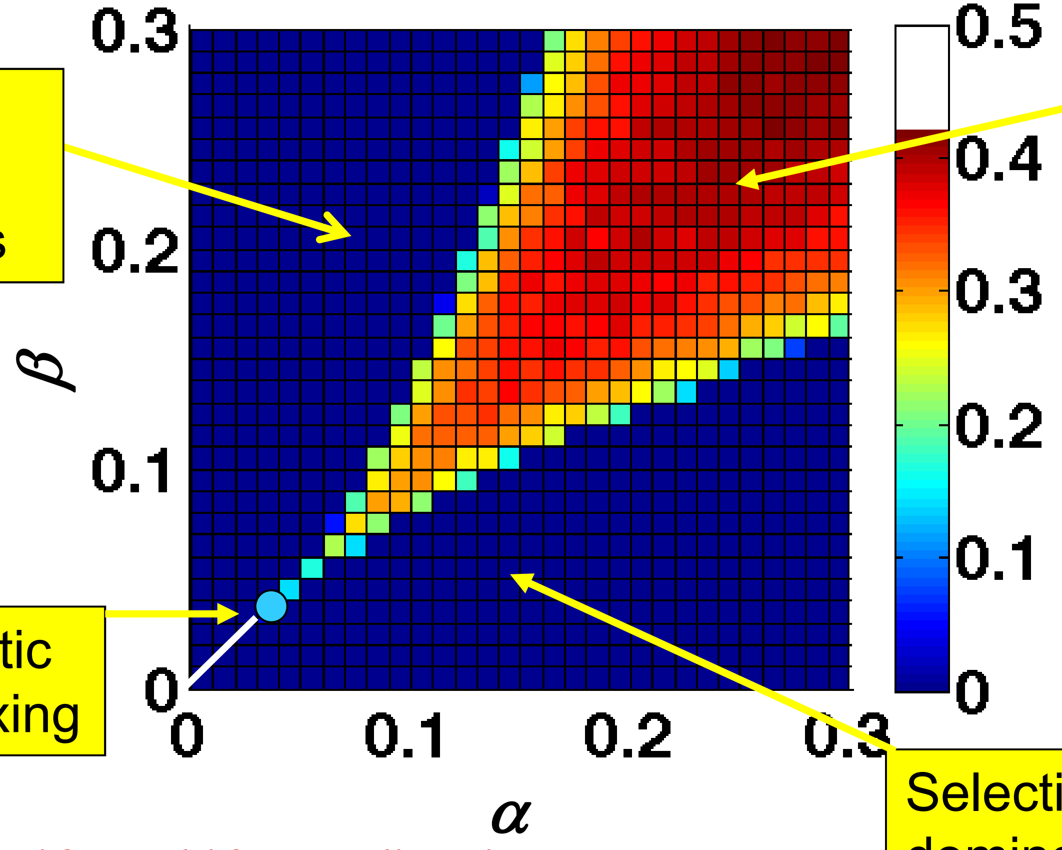
Effect of genetic drift for α > 0, β > 0

$$\frac{\partial f(x,t)}{\partial t} = D\frac{\partial^2 f(x,t)}{\partial x^2} + s_0(f^* - f)f(1-f) + \boxed{\sqrt{f(1-f)/2N}\;\Gamma(x,t)}$$

Selective dominance:
Blue prevails

Mutualism prevails

Genetic demixing



Selective dominance:
Yellow prevails

Genetic drift, i.e., number fluctuations, reduces the domain of mutualism from the entire first quadrant

What happens if we shift mutalism into <u>competitive exclusion</u>, i.e. a < 0 & β < 0 → antagonistic interactions ??

Pushed Genetic Waves and Antagonistic Interactions

Andrea Giometto

- *For pushed genetic waves, a "critical nucleus" is required to excite the wave to get it started (like nucleation theory)*

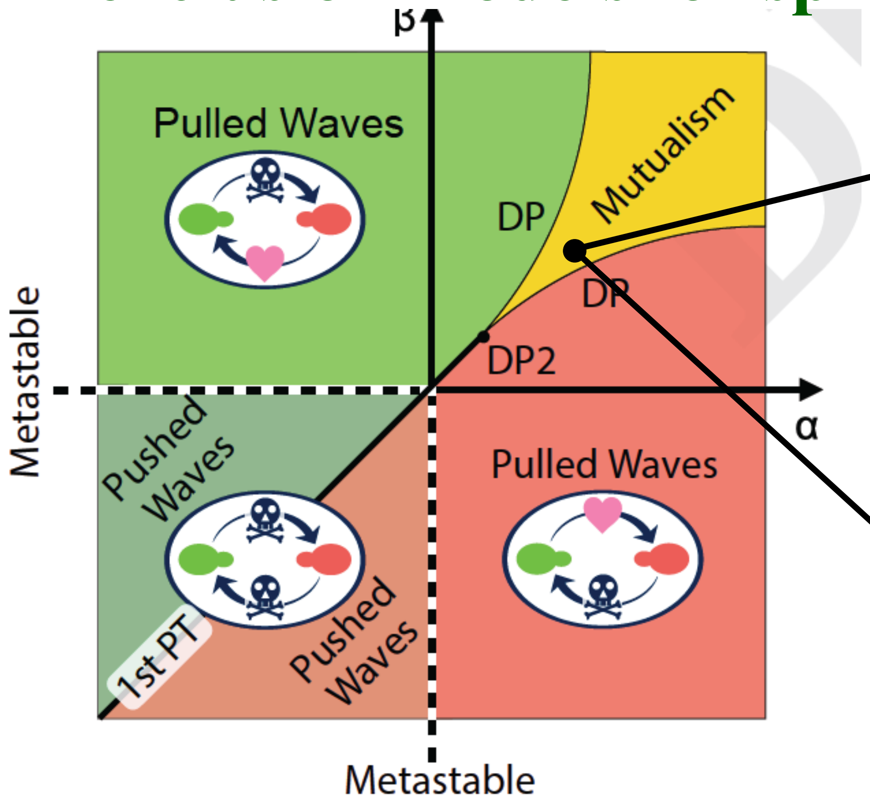
Andrew Murray

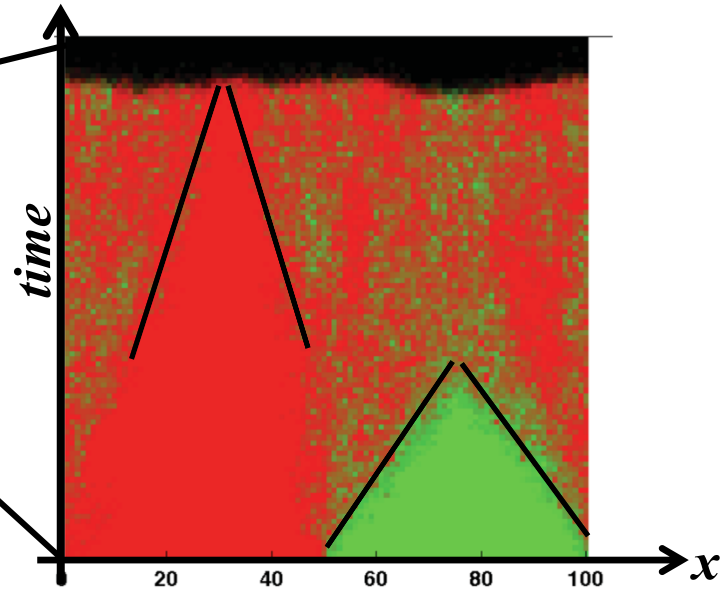
- *How can an excitable pushed wave from a gene drive be stopped? (They are fragile and can be stopped by obstacles….)*

Max Lavrentovich
Univ. of Tennessee

- *Can we detect the existence of a critical nucleus with killer yeast or bacteria strains? (project with Andrea & Andrew)*

Summary: Pushed waves appear in competitive exclusion models for spatial evolutionary games





Mutualistic "Smoke" propagates via a pulled Fisher wave (Kirill Korolev)

- *Fisher genetic waves are "pulled waves", driven by growth and diffusive dispersal at the leading edge.*
- *Excitable genetic waves are "pushed waves", driven by populations behind the front whose offspring spill over to the leading edge → strong "Allee effect" (A. Stokes, 1976)*

Frequency dependent selection

If w_B and w_Y are the reproduction rates of blue and yellow produced during one generation at a given point on the frontier...

selective advantage $s(f) \approx \dfrac{w_B - w_Y}{(w_B + w_Y)/2}$

If $f(x,t)$ = yellow fraction, 1- $f(x,t)$ = blue fraction

describe mutualism by...

$$w_Y(x,t) = [1 + \beta(1 - f(x,t))]/\tau_g$$

$$w_B(x,t) = [1 + \alpha f(x,t)]/\tau_g$$

τ_g = generation time

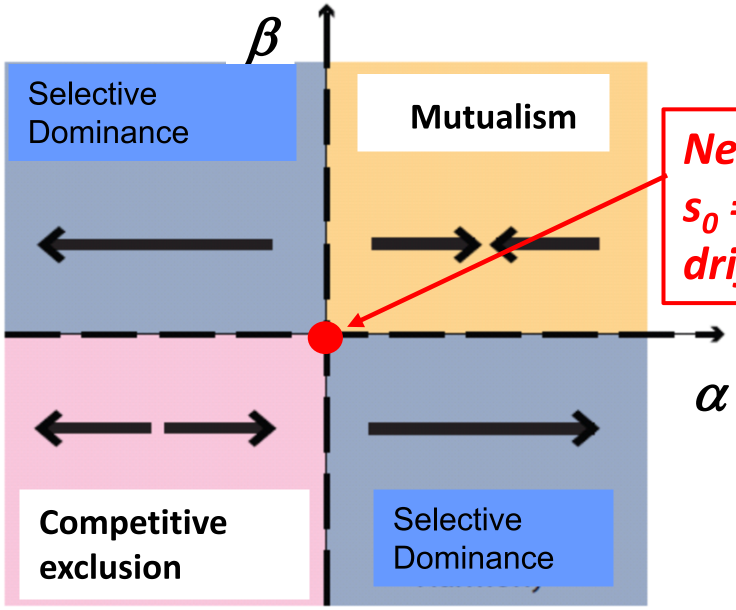
$$s(f) \approx s_0(f^* - f)$$

$$s_0 = \alpha + \beta$$

$$f^* = \beta/(\alpha + \beta)$$

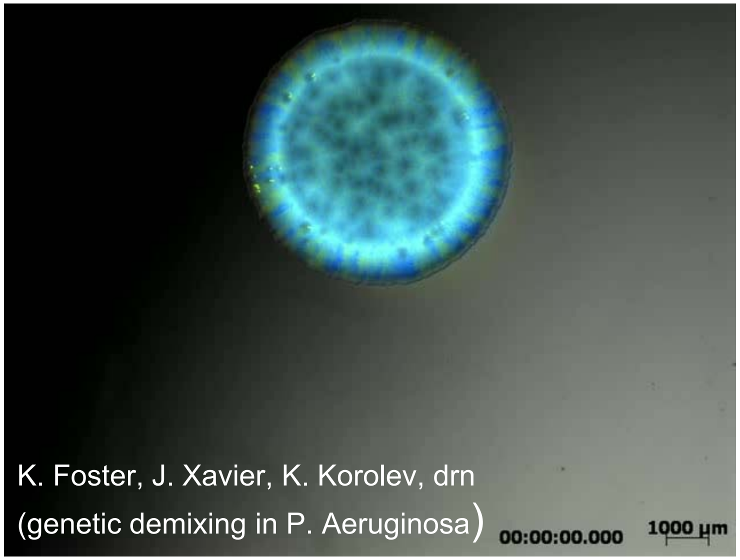
$$\frac{\partial f(x,t)}{\partial t} = D\frac{\partial^2 f(x,t)}{\partial x^2} + s_0(f^* - f)f(1-f)$$

+ number fluctuations



Neutral model
$s_0 = 0$, genetic drift important

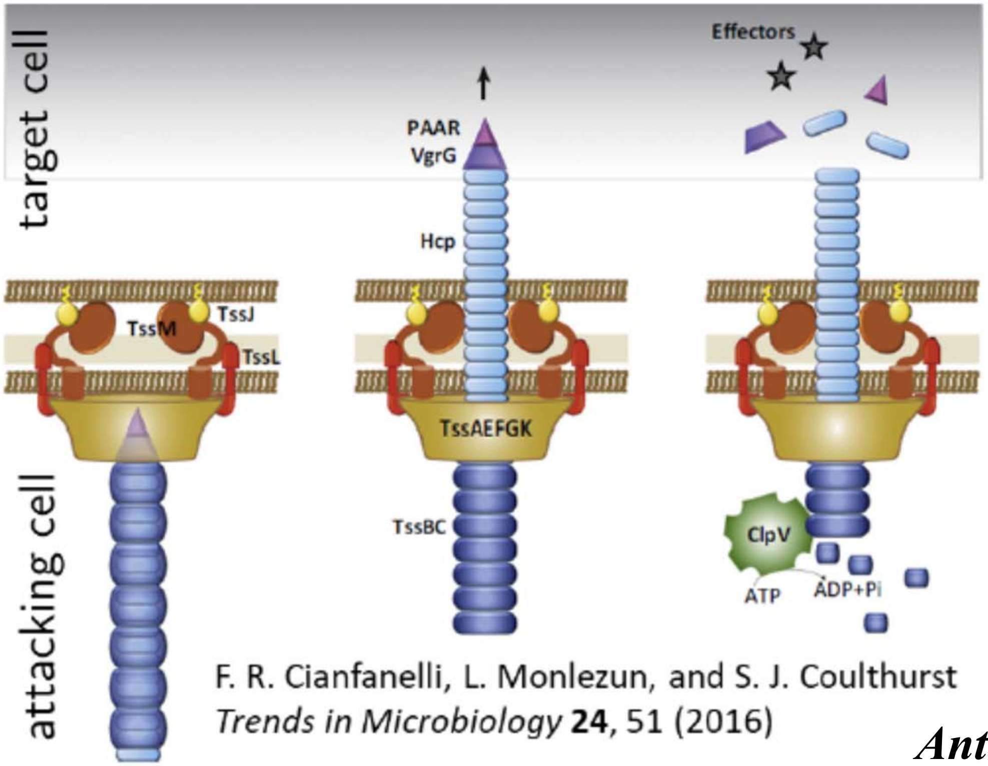
M. Nowak et al., Nature (2004)
J. Gore et al. Nature (2009)
E. Frey et al., Phys. Rev. Lett. (2010)



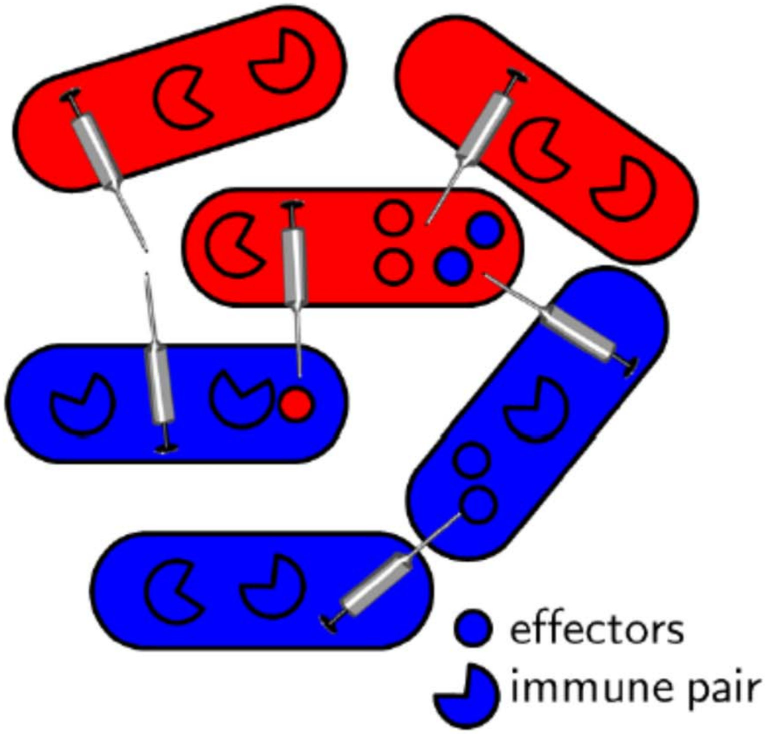
K. Foster, J. Xavier, K. Korolev, drn (genetic demixing in P. Aeruginosa)

What happens for both α & β negative?

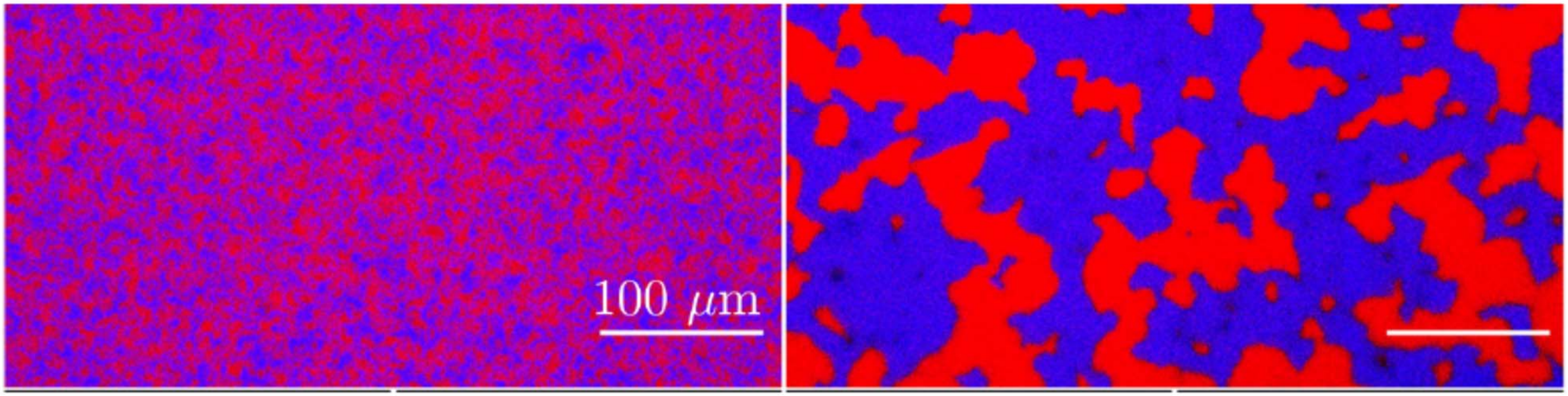
Antagonistic interactions $(\alpha, \beta < 0)$: type VI secretion



F. R. Cianfanelli, L. Monlezun, and S. J. Coulthurst
Trends in Microbiology **24**, 51 (2016)



Antagonism-induced coarsening

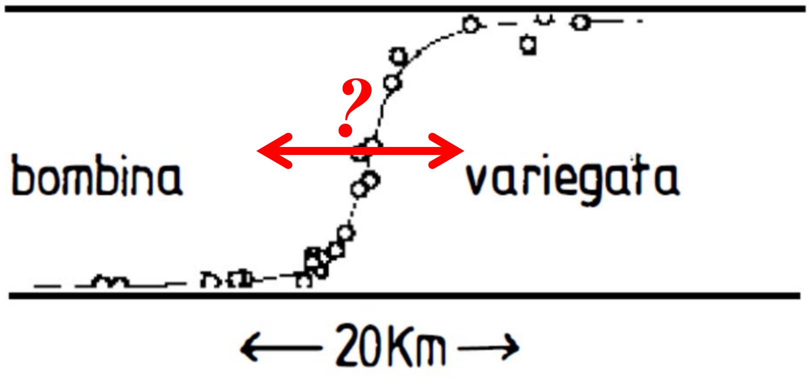


L. McNally et al., *Nature Communications* **8**, 14371 (2016)

Pushed genetic waves in “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*

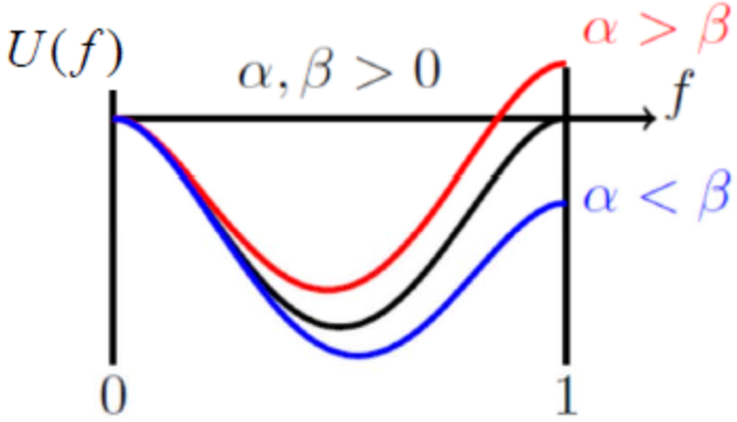
A course-grained description: diffusion in a potential

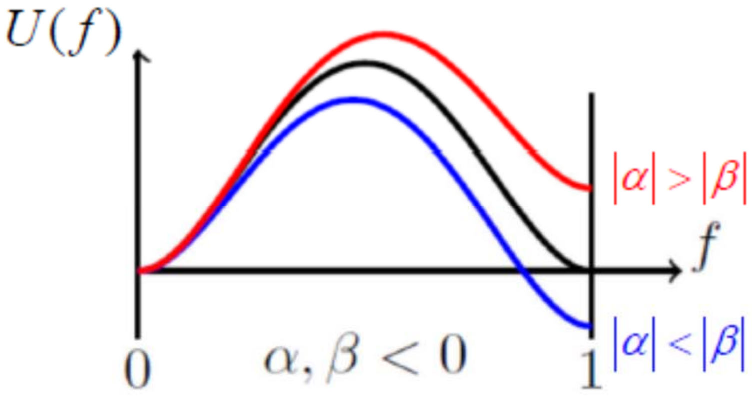
Consider an allele fraction $f \equiv f(\mathbf{x}, t)$ at position $\mathbf{x}$ and time t. Then:

$$\partial_t f = D_s \nabla^2_{\mathbf{x}} f + \frac{f(1-f)}{\tau_g}\left[(\alpha+\beta)\left(\frac{1}{2}-f\right)+\frac{\alpha-\beta}{2}\right] + \sqrt{\frac{2f(1-f)}{N\tau_g}}\,\xi$$

$$= D_s \nabla^2_{\mathbf{x}} f - \frac{1}{\tau_g}\frac{dU(f)}{df} + \sqrt{D_g f(1-f)}\,\xi$$ with number fluctuations:

$\langle \xi(\mathbf{x}, t) \rangle = 0$ and $\langle \xi(\mathbf{x}, t)\xi(\mathbf{x}', t') \rangle = \delta(t-t')\delta(\mathbf{x}-\mathbf{x}')$.





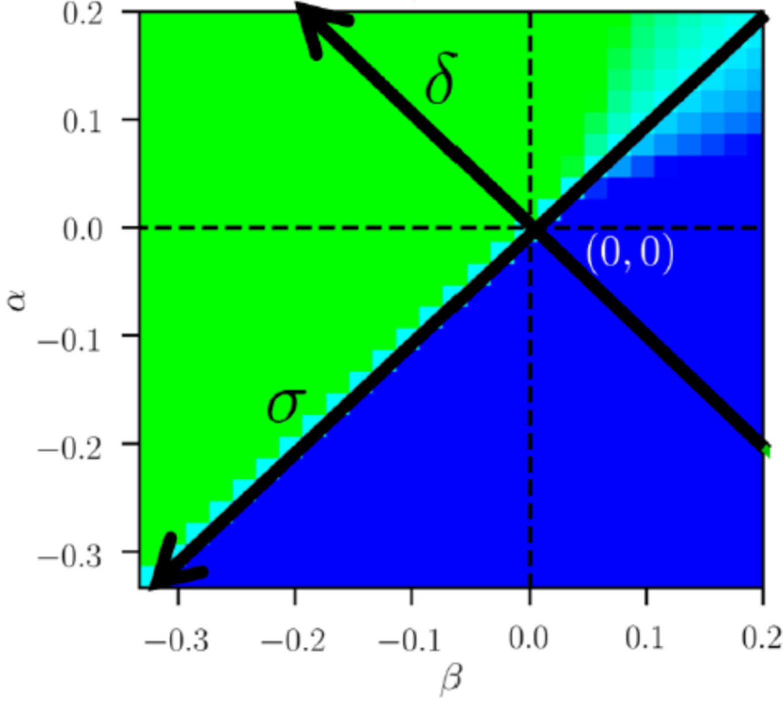
go to board 3

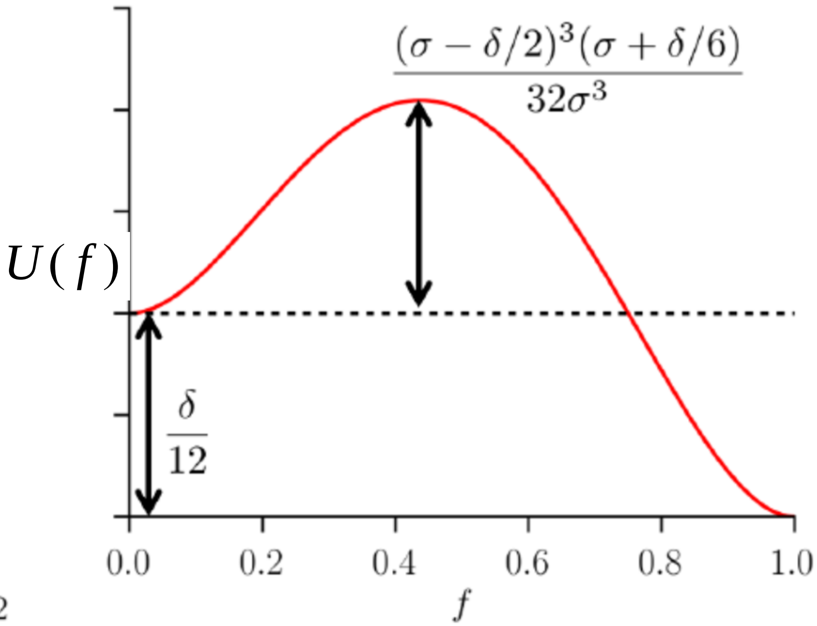
A convenient reparameterization

To study the antagonistic interactions in the third quadrant, we rotate our coordinates to $\sigma = -(\alpha + \beta)/2$ and $\delta = \alpha - \beta$:

$$\partial_t f = D_s \nabla^2 f + f(1-f)\left[\sigma(2f-1) + \frac{\delta}{2}\right] + \sqrt{D_g f(1-f)}\,\xi \tag{1}$$

$\delta = \alpha - \beta =$ selective advantage; $\sigma = (\alpha + \beta)/2 =$ "antagonism"





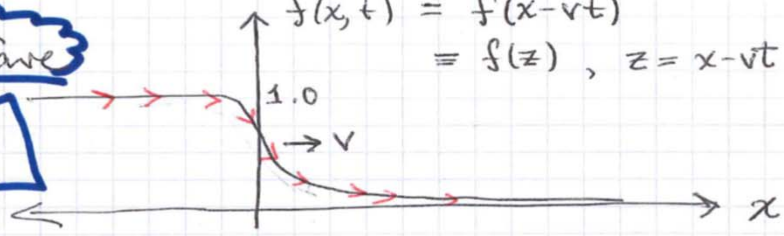
"Model A" with nonlinear noise!

Dynamical Systems Approach to Pushed & Pulled Waves

① Simple Pulled Fisher Wave

$$\boxed{\frac{\partial f}{\partial t} = D\frac{\partial^2}{\partial x^2}f + s\, f(1-f) \equiv D\frac{\partial^2}{\partial x^2}f + \frac{dV(f)}{df}}$$

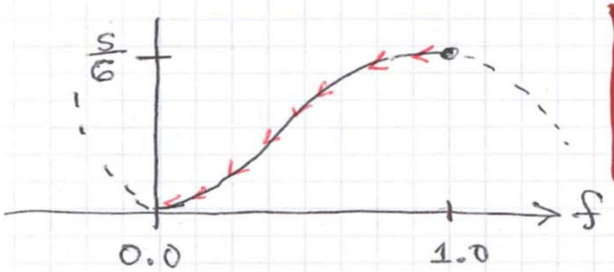
$$f(x,t) = f(x-vt) = f(z)\,,\quad z = x-vt$$



$$V(f) = \tfrac{1}{2}s\,f^2 - \tfrac{1}{3}s\,f^3$$

becomes

$$\boxed{\underset{\uparrow\ \text{"mass"}}{D}\,\ddot{f}(z) = \underset{\uparrow\ \text{"damping"}}{-v}\,\dot{f}(z) - \underset{\text{"potential energy"}}{\frac{dV(f)}{df}}} \quad ✪$$



Indeed, multiply ✪ by $\dot{f}(z)$ & integrate to get

$$\boxed{\int_{-\infty}^{\infty} dz\, \frac{d}{dz}\underbrace{\left\{\tfrac{1}{2}D\left(\frac{df}{dz}\right)^2 + V(f)\right\}}_{\text{kinetic \& potential energy}} = -v\underbrace{\int_{-\infty}^{\infty}\left(\frac{df}{dz}\right)^2 dz}_{\text{dissipation}}}$$

OR

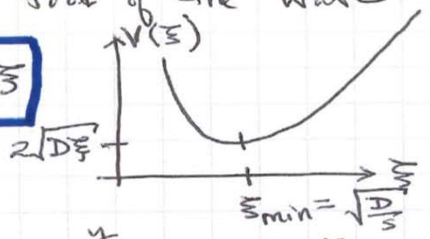
$$\left[\tfrac{1}{2}D\left(\frac{df}{dz}\right)^2 + V(f)\right]_{-\infty}^{\infty} = -\frac{s}{6} \Rightarrow \boxed{v = \frac{s}{6\int_{-\infty}^{\infty}\left(\frac{df}{dz}\right)^2 dz}} \quad ✱$$

✱ Try $\boxed{f(z) = \tfrac{1}{2} - \tfrac{1}{2}\tanh(z/2\xi) \underset{z\to\infty}{\approx} e^{-z/\xi}}$

velocity changes direction when s changes

* With this ansatz, we find, at the foot of the wave

$$\frac{D}{\xi^2} = \frac{v}{\xi} - s \Rightarrow \boxed{v = \frac{D}{\xi} + s\xi}$$



& from our "variational ansatz",

we have $$\int_{-\infty}^{\infty}\left(\frac{df}{dz}\right)^2 dz = \frac{1}{16\xi^2}\int_{-\infty}^{\infty} dz\, \text{sech}^4(\overset{y}{\widetilde{z/2\xi}}) = \frac{1}{8\xi}\underbrace{\int_{-\infty}^{\infty} dy\, \text{sech}^4(y)}_{4/3\ (!)}$$

(see Wolfram alpha)

so $$\int_{-\infty}^{\infty}\left(\frac{df}{dz}\right)^2 dz = \frac{1}{6\xi}$$ & so $\divideontimes$ gives

$$\boxed{v = s\xi} \Leftarrow$$ not quite right if $v = 2\sqrt{Ds}$, $\xi = \sqrt{\frac{D}{s}}$

since then $2\sqrt{Ds} = \sqrt{Ds} \Rightarrow 2 = 1$!

* Need better variational ansatz!

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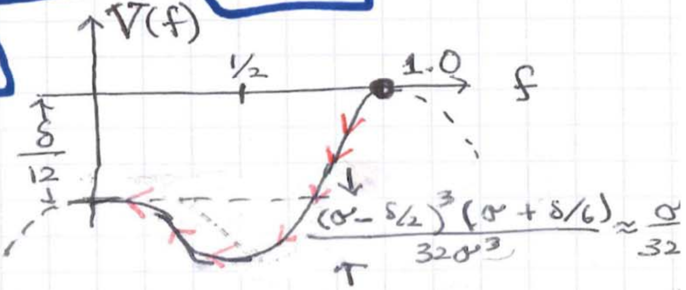
③ **Excitable Pushed Wave** for $\alpha, \beta < 0$, $\delta = \alpha - \beta$, $\sigma = \frac{-(\alpha+\beta)}{2}$

we had

$$\boxed{\begin{aligned}\frac{\partial f}{\partial t} &= D\frac{\partial^2 f}{\partial x^2} + \frac{2\sigma}{\tau_g} f(1-f)\left(f - \frac{1}{2} - \frac{\delta}{4\sigma}\right)\\ &\equiv D\frac{\partial^2}{\partial x^2}f + \frac{dV(f)}{df}\end{aligned}}$$



Proceeding as before, we have

$$\boxed{v = \frac{\delta}{12\int_{-\infty}^{\infty}\left(\frac{df}{dz}\right)^2 dz}}$$

so wave again changes direction, this time when $\underline{\underline{\underline{\delta}}}$ changes sign!

("friction" embodied in the velocity v, allows a smooth approach to extremum a $f = 0$ as $z \to +\infty$)

Double well potential, nucleation theory and Maxwell construction

Recast dynamics in terms of a functional derivative:

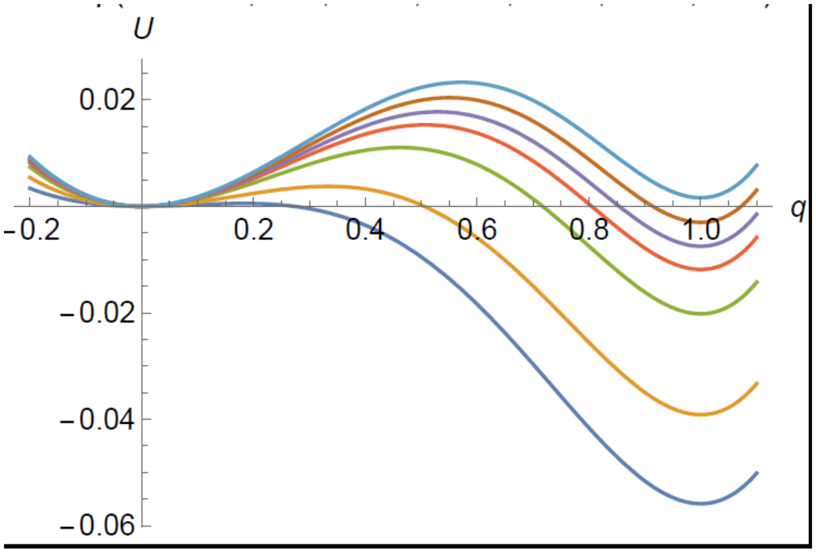
$$\frac{\partial f(x,t)}{\partial t} = -\frac{\delta F}{\delta f(x,t)}, \quad F(t) = \int_{-\infty}^{\infty} \left[\frac{1}{2}\tau_g D \left(\frac{\partial f(y,t)}{\partial y} \right)^2 + U[f(y,t)] \right] dy$$

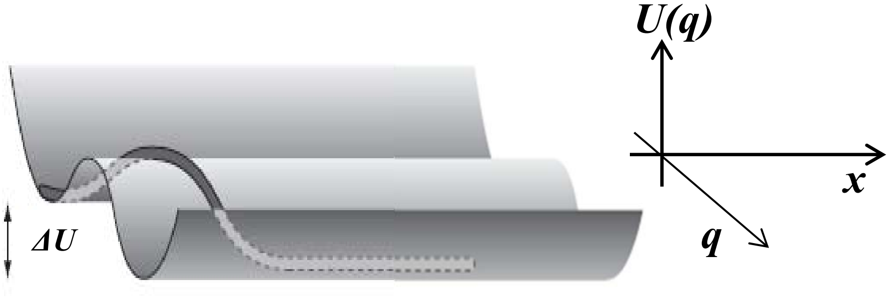
$$U(f) = -\frac{1}{\tau_g} \int_0^q 2\sigma f(1-f)(f-f^*)\,dq$$

Can show that the dynamics is such that $F(t)$ always decreases:

$$\frac{dF(t)}{dt} = -\int_{-\infty}^{\infty} \left(\frac{\partial f(x,t)}{\partial t} \right)^2 dx < 0$$

[$U(q)$ has a double well structure...]





Pushed waves requiring a critical nucleus stall out when the two minima have the same depth

go to board 4

Pushed Fisher waves for α, β < 0

$$\frac{\partial f(x,t)}{\partial t} \approx D\nabla^2 f + \left(2\sigma/\tau_g\right) f(1-f)(f-f^*);\; f^* = \frac{1}{2} - \frac{\delta}{4\sigma},$$

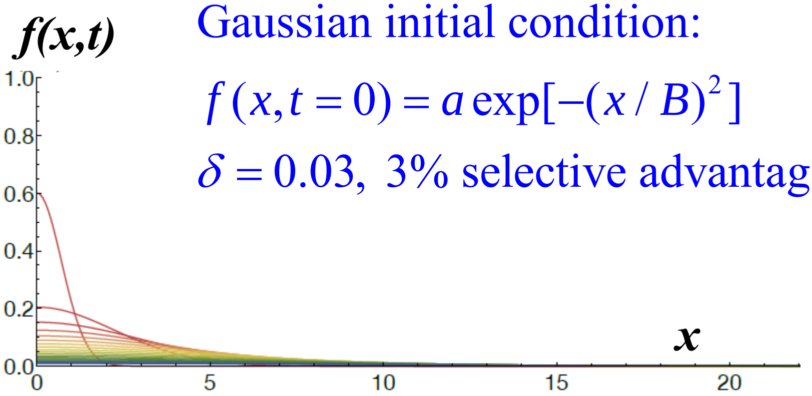
an exact traveling wave solution exists!

$$f(x,t) = \frac{1}{1+\exp[(x-v_E t)\sqrt{\sigma/\tau_g D}]};\quad v_E = \frac{1}{2}\frac{\delta}{\sigma}\sqrt{D/\tau_g};\quad \delta << \sigma$$

N. H. Barton & M. Turelli,
The American Naturalist
178, E48 (2011)

*A "critical propagule" size for the gene drive is required to nucleate the wave

*Wave reverses direction when $\delta = \alpha - \beta$ changes sign

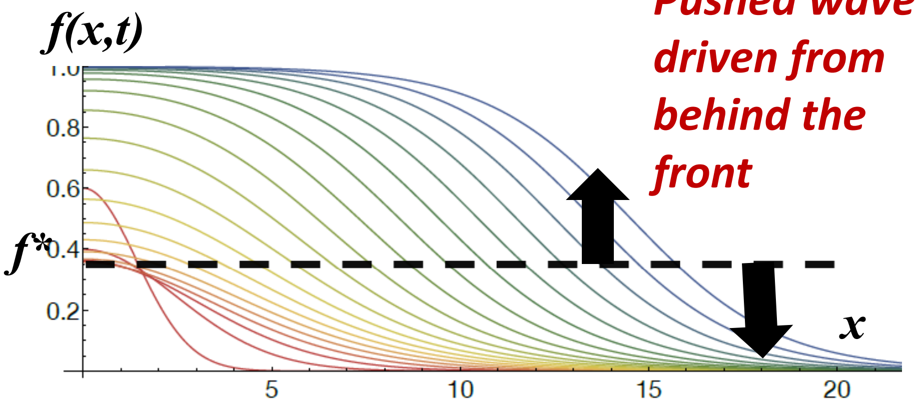


Gaussian initial condition:

$$f(x,t=0) = a\exp[-(x/B)^2]$$

$\delta = 0.03$, 3% selective advantage

(a) Too small to nucleate: $a = 0.6, B = 1.0$



Pushed wave driven from behind the front

(b) Successful nucleation: $a = 0.6, B = 2.0$

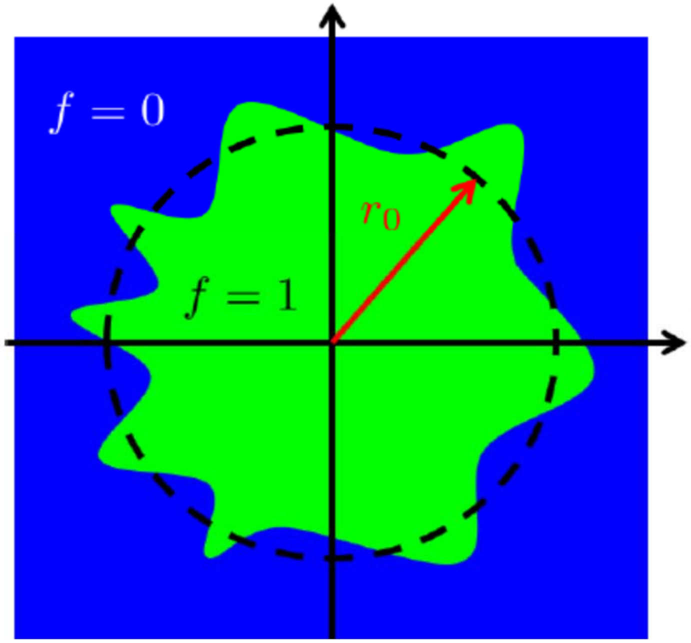
Nucleation has an even more dramatic effect in two dimensions

Nucleation and growth for $\delta > 0$, $\sigma \geq 0$

Suppose we look at droplets with $0 < \delta \ll \sigma$. The "energy" of such a drop is

$$E[f] = \int \mathrm{d}\mathbf{x} \left[\frac{D_s}{2} (\nabla f)^2 + U(f) \right]$$

We can look for minimal $E[f]$ solutions that look like droplets:



$$\nabla^2 f = -\frac{\sigma}{D_s} f(1-f)(2f-1)$$

⇓

$$f(r) = \frac{1}{2} - \frac{1}{2} \tanh \left[\sqrt{\frac{\sigma}{4D_s}} (r - r_0) \right]$$

⇓

$$E = 2\pi r_0 \underbrace{\left[\frac{1}{12} \sqrt{D_s \sigma} \right]}_{\text{line tension}} - \pi r_0^2 \underbrace{\left[\frac{\delta}{12} \right]}_{\text{condensation energy}}$$

Test of nucleation theory in two dimensions

Xiaojue Zhu,
R. Benzi,
F. Toschi & drn

droplet energy $E(R) = 2\pi R\gamma - \pi c R^2$,

line tension γ=(2/3)$\sqrt{\sigma/\mathrm{D}}$, condensation energy $c = \delta / 3D$

critical droplet size $= R_c = \gamma / c = (2/\delta)\sqrt{D\sigma}$

The dynamics of the droplet radius $R(t)$ is given by

$$\frac{dR(t)}{dt} = -\frac{D}{R(t)} + \frac{\delta}{2}\sqrt{\frac{D}{\sigma}} \quad \text{(require } R(t) >> w = \text{ interface width)}$$

→ critical droplet radius $R_c = \gamma / c = (2/\delta)\sqrt{D\sigma}$

→ dying droplets should vanish with a square root singularity,

$$R(t) = \sqrt{R_0^2 - 2D(t - t_0)},$$

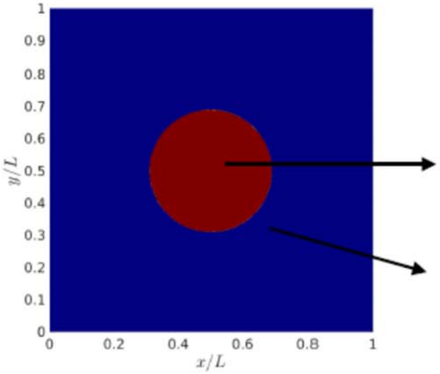
where R_0 is the radius of a dying droplet has well below the maximum R_c at time t_0

→ Once the droplet is above the maximum, we should eventually have a circular, expanding pushed wave with $R(t) \approx vt,\ v = (\delta / 2)\sqrt{D/\sigma}$

simulations: selective advantage = $\delta = \varepsilon_A - \varepsilon_B = 0.1$

antagonism = $\sigma = -(\varepsilon_A + \varepsilon_B)/2 = 0.25$

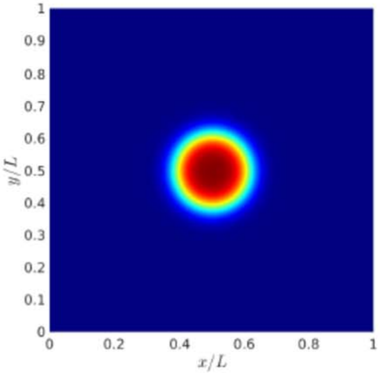
2. Initial radius=0.12 without flow



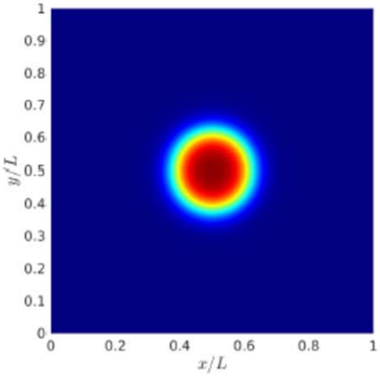
$c_A = 1, c_B = 0$

$c_A = 0, c_B = 1$

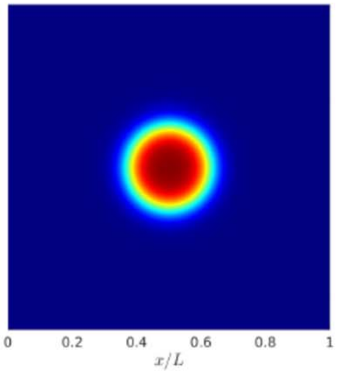
t=0



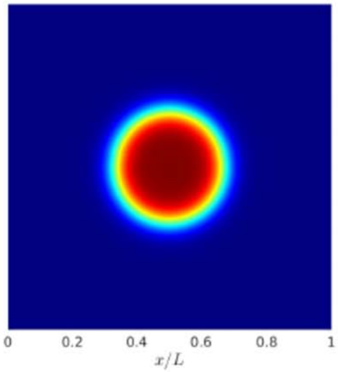
t=10



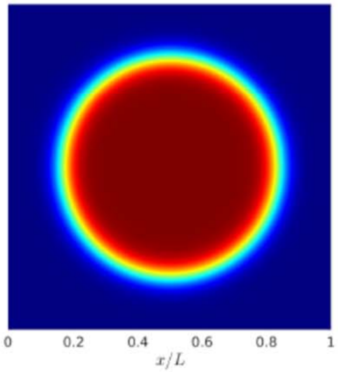
t=100



t=200

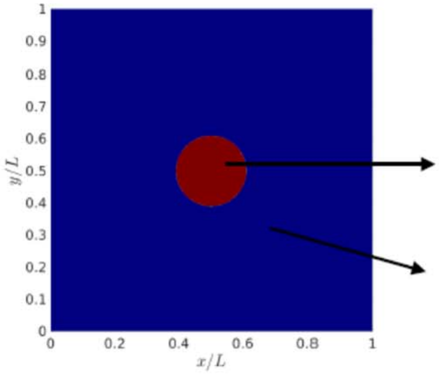


t=400



t=756

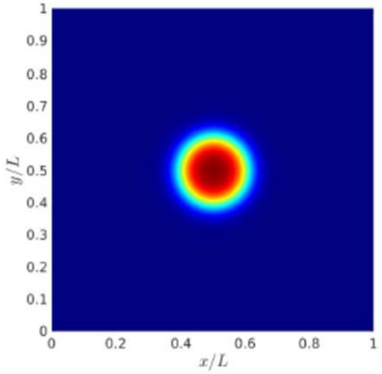
1. Initial radius=0.11 without flow



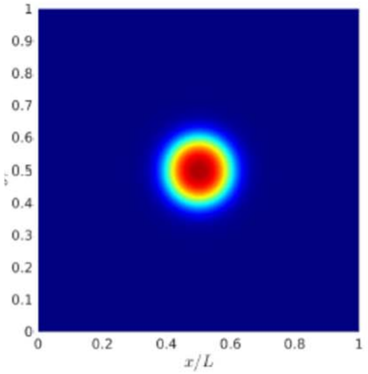
$c_A = 1, c_B = 0$

$c_A = 0, c_B = 1$

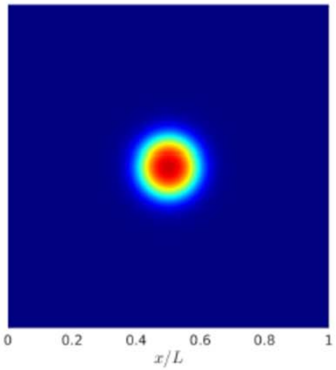
t=0



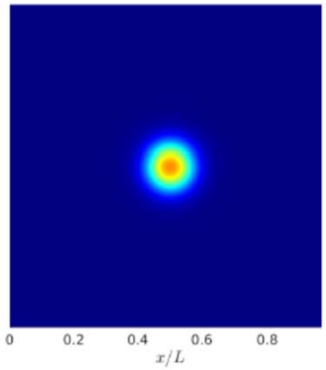
t=10



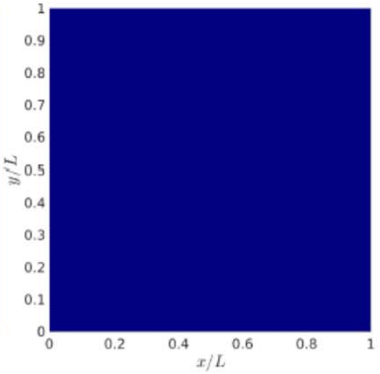
t=100



t=150

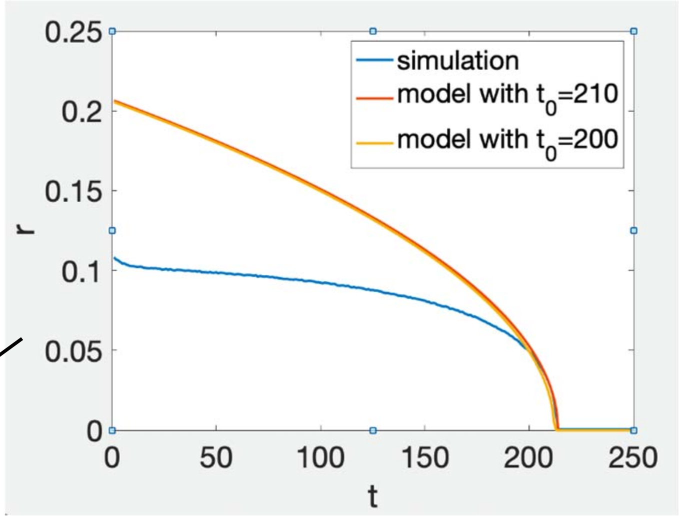


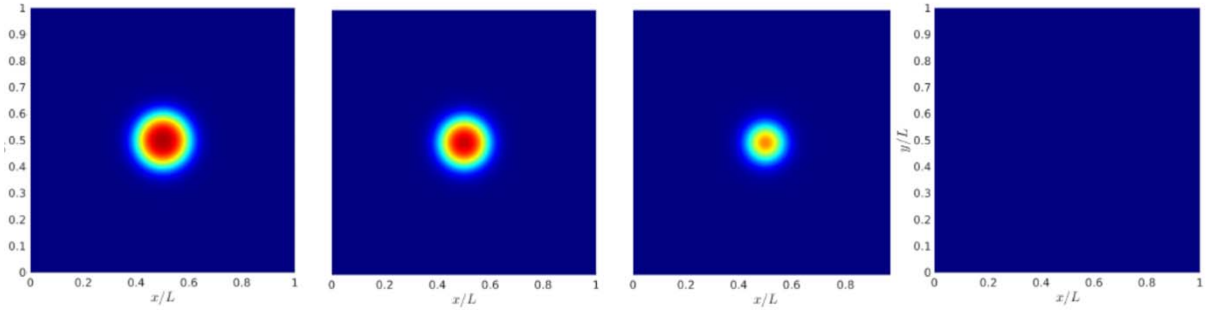
t=200



t=300

Test of critical radius prediction from simulations

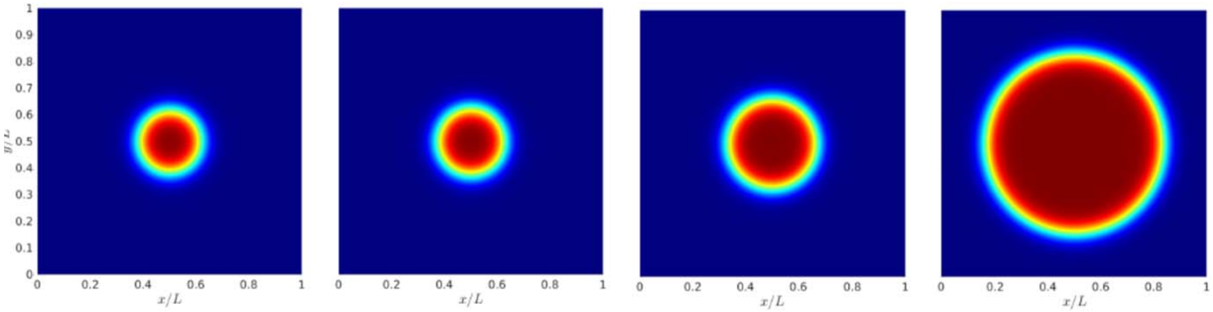




t=100 **t=150** **t=200** **t=300**

Initial radius=0.11 without flow

$R < R_c$



t=100 **t=200** **t=400** **t=756**

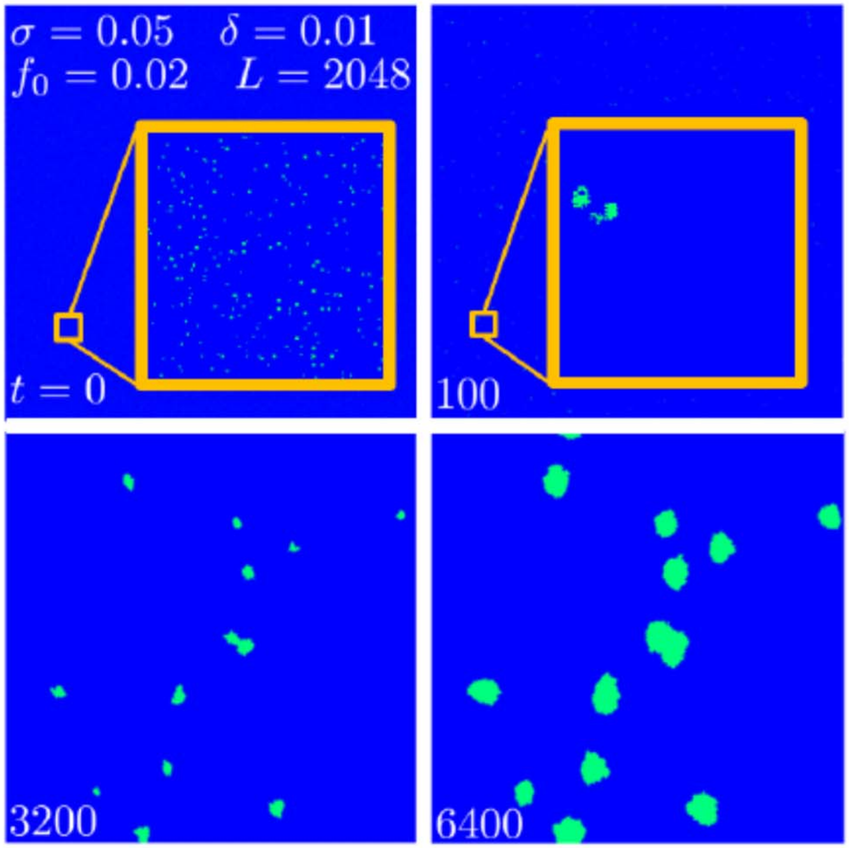
Initial radius=0.12 without flow

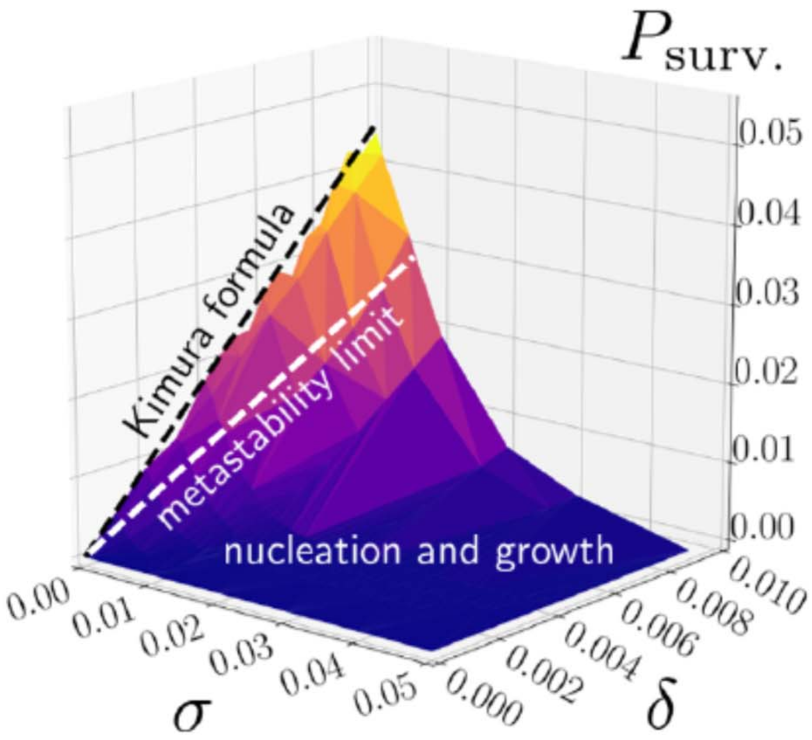
$R > R_c$

Green cells must overcome line tension to grow

$$\sigma = -(\alpha+\beta)/2, \quad \delta = \alpha - \beta, \quad \delta \ll \sigma \ll 1$$

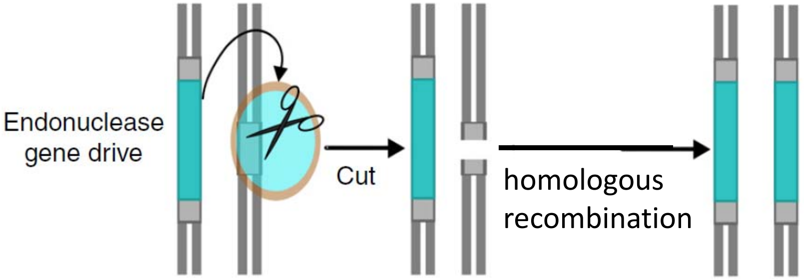
Nucleation theory ideas can be used to compute the survival probability in this limit





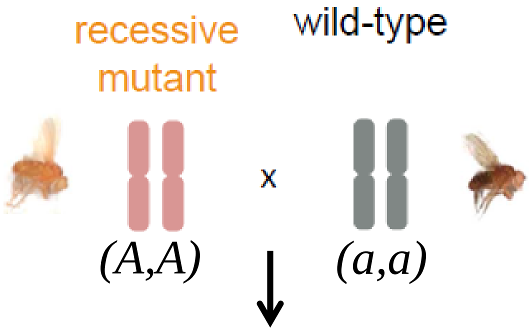
C. R. Doering, C. Mueller, and P. Smereka, *Physica A* **325**, 243 (2003)
T. Maruyama, *Theor. Popul. Biol.* **5**, 148 (1974)

Relevance to CRISPR-Cas9 gene drives & non-Mendelian population genetics



R. L. Unckless, A. G. Clark, and P. W. Messer, Genetics 205.2 (2017): 827-841.

Classical Mendelian inheritance: 50% in F_1

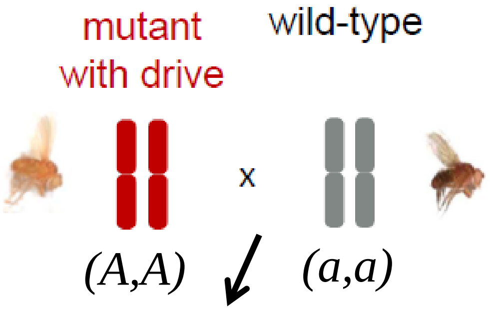


$$\begin{array}{cc} & \begin{array}{cc} a & a \end{array} \\ \begin{array}{c} A \\ A \end{array} & \begin{pmatrix} Aa & Aa \\ Aa & Aa \end{pmatrix} \end{array}$$

The offspring are heterozygous, and they display the wild type phenotype if dominant

vs.

Gene-driven inheritance: 100% in F_1

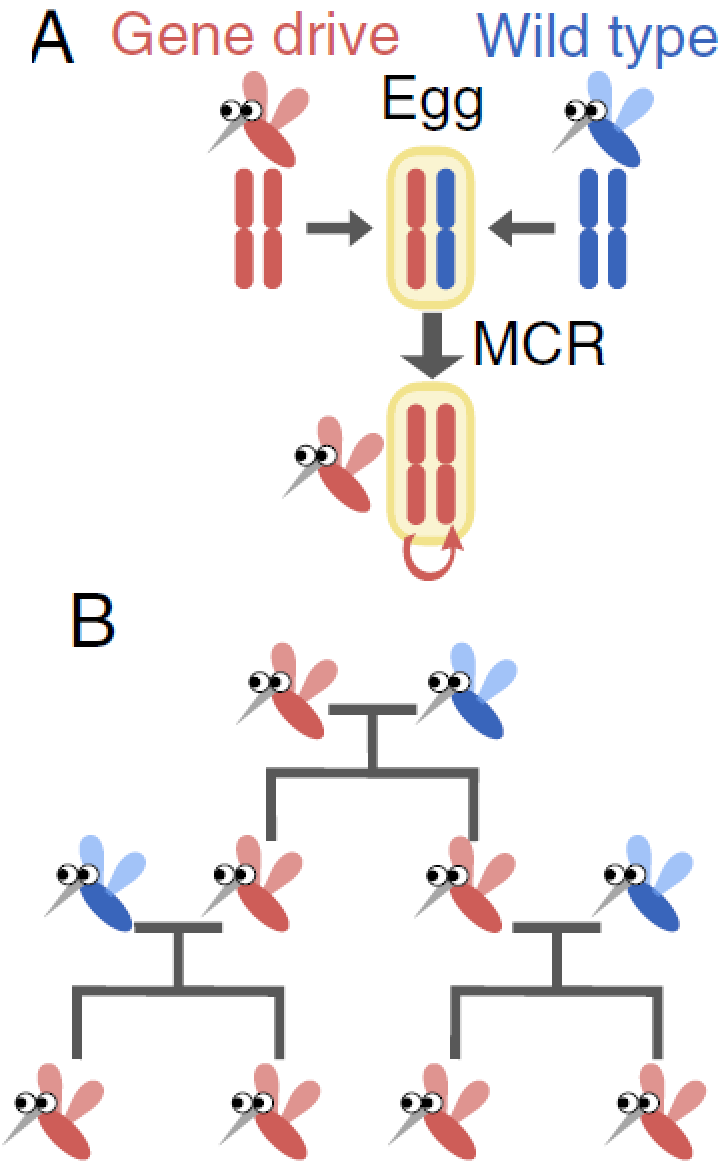


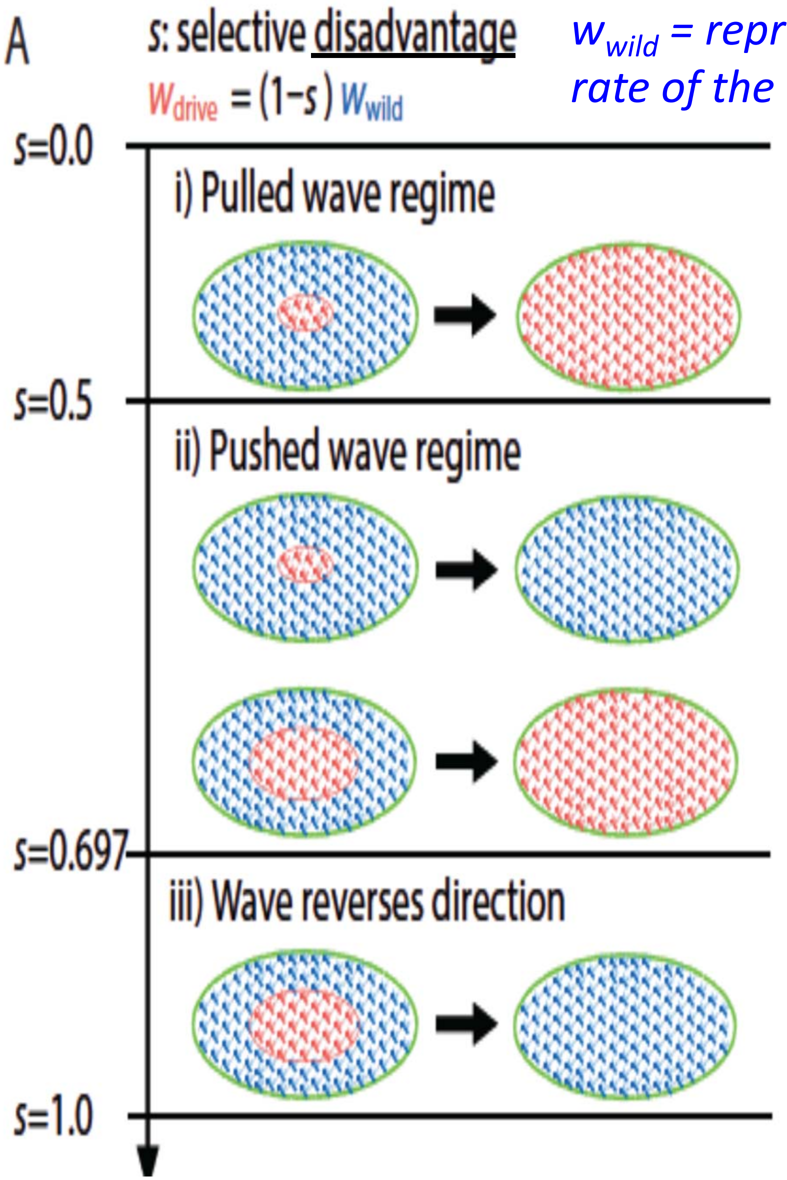
$$\begin{array}{cc} & \begin{array}{cc} a & a \end{array} \\ \begin{array}{c} A \\ A \end{array} & \begin{pmatrix} Aa & Aa \\ Aa & Aa \end{pmatrix} \end{array} \rightarrow \begin{array}{cc} & \begin{array}{cc} a & a \end{array} \\ \begin{array}{c} A \\ A \end{array} & \begin{pmatrix} AA & AA \\ AA & AA \end{pmatrix} \end{array}$$

!

Nearly 100% conversation to homozyotes with the gene drive reported for flies & yeast…. (neglect non-homologous end joining)

Spatial spread of pushed and pulled genetic waves

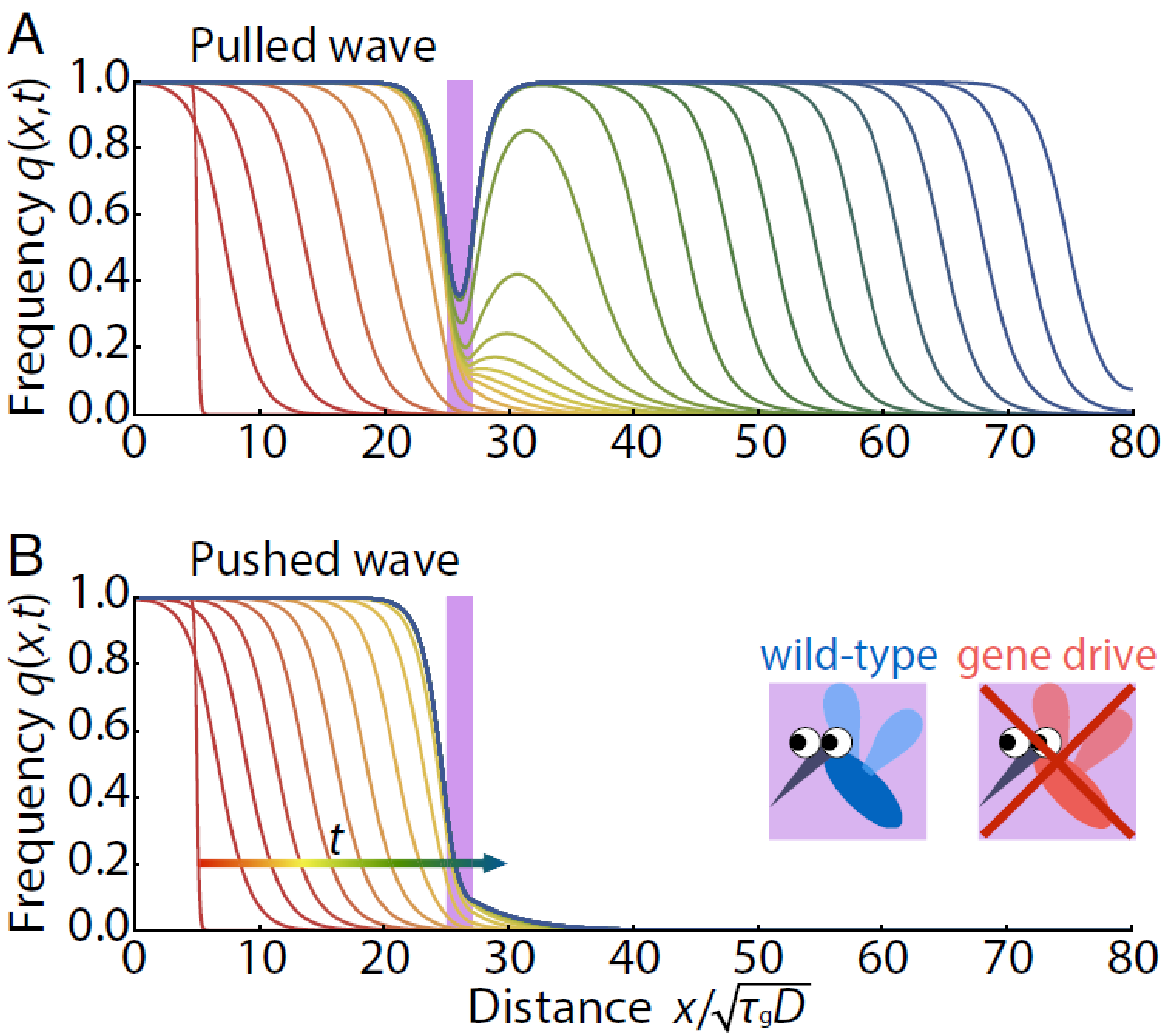




w_{wild} = reproduction rate of the wild type

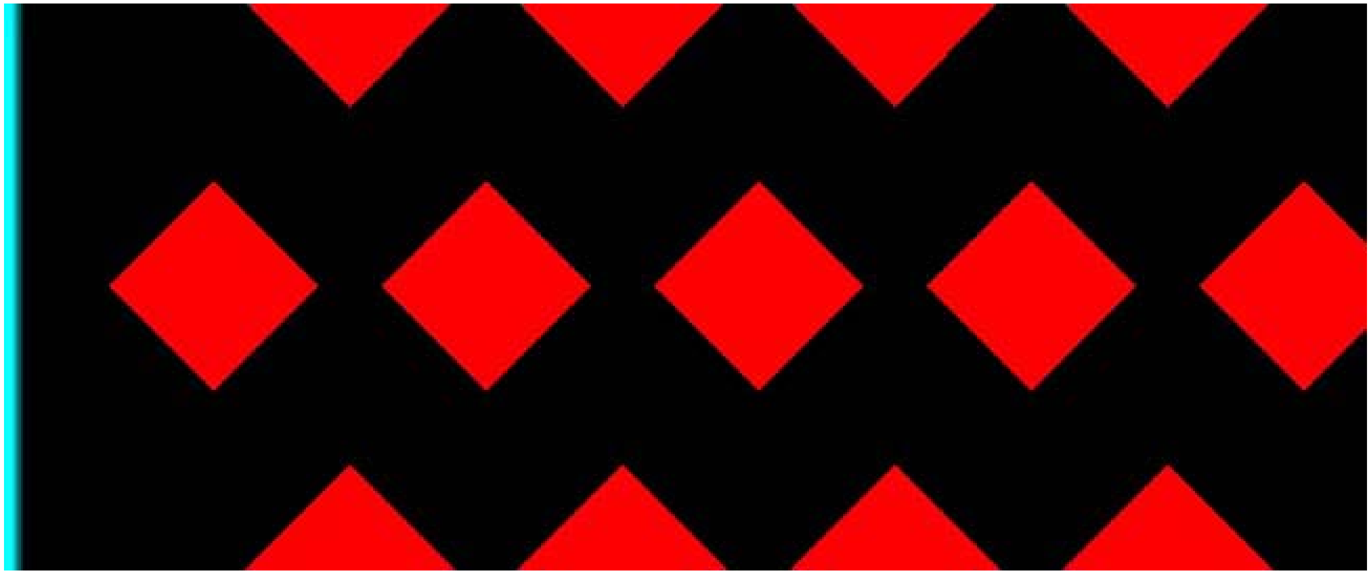
The effect of obstacles: Pushed, excitable waves are more fragile than their pulled Fisher wave counterparts…

Stopping power of a selective disadvantage barrier in one dimension



In two dimensions, conventional Fisher waves easily traverse an array of obstacles

Simulations by
W. Moebius,
drn & A. Murray



For dilute arrays, the cusps heal and the propagation velocity is unchanged

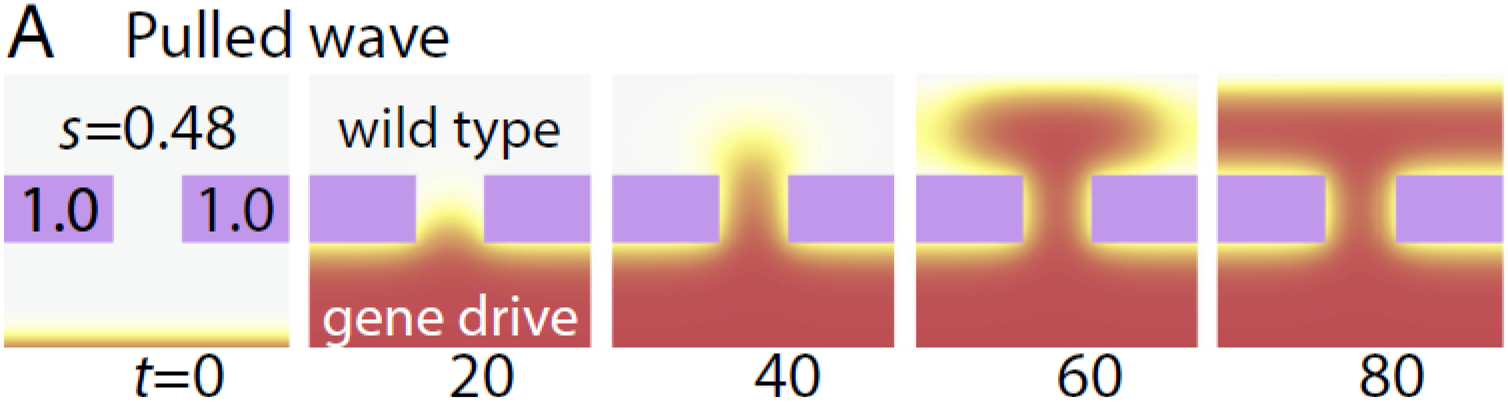
But pushed waves are more fragile!

A dense array of obstacles merely leads to a reduced propagation velocity --

Stopping power of selective disadvantage barriers in two dimensions

$$\frac{\partial f(\vec{x},t)}{\partial t} \approx D\nabla^2 f + \left(2\sigma/\tau_g\right) f(1-f)(f-f^*) + \text{genetic drift}, \quad f^* = 1/2 + \delta/4\sigma$$

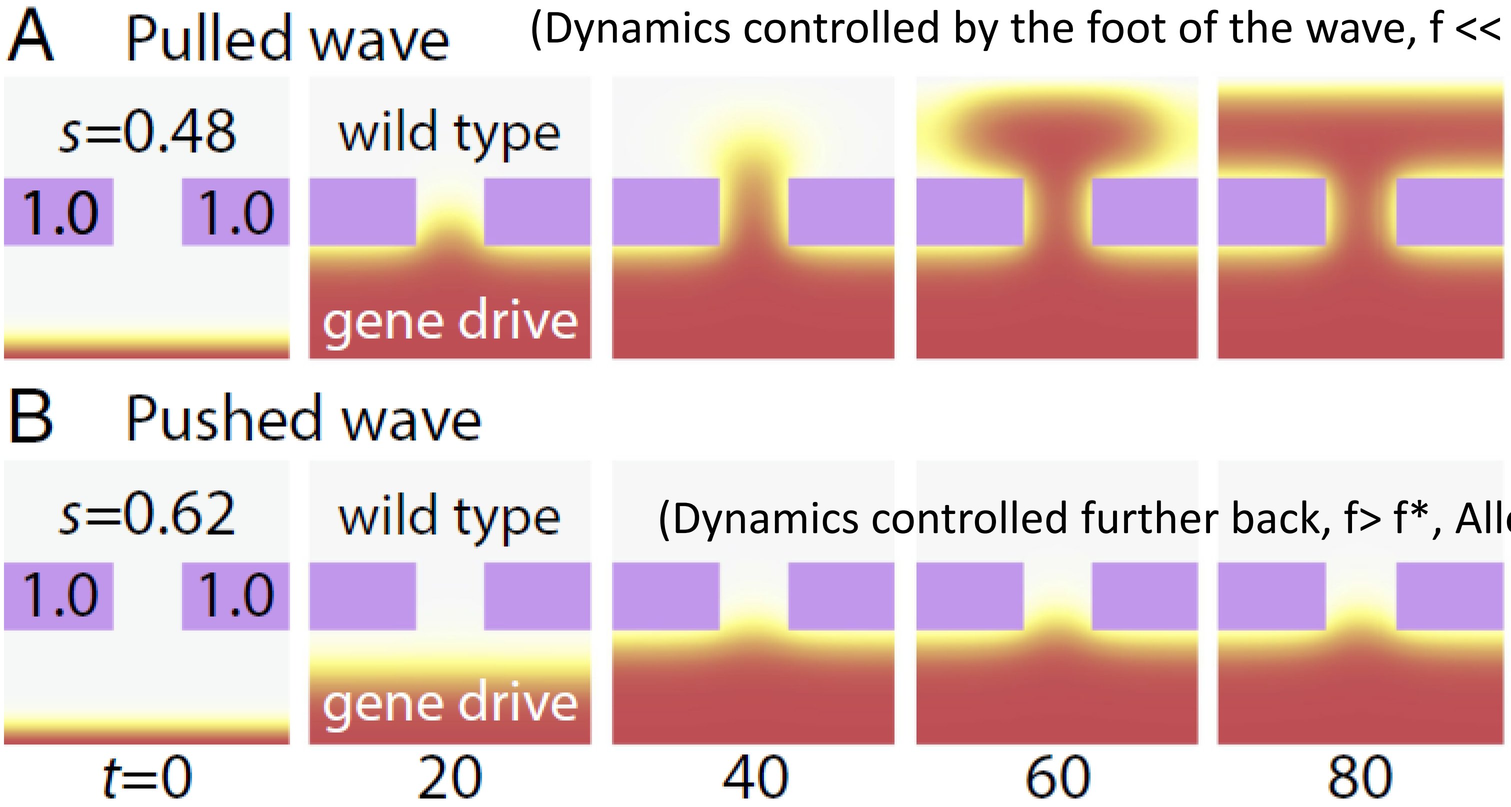
$f(\vec{x},t) =$ concentration of gene drive homozygotes at position $\vec{x}$ and time t



Stopping power of selective disadvantage barriers in two dimensions

$$\frac{\partial f(\vec{x},t)}{\partial t} \approx D\nabla^2 f + \left(2\sigma/\tau_g\right) f(1-f)(f-f^*) + \text{ genetic drift}$$

$f(\vec{x},t) =$ concentration of gene drive homozygotes at position $\vec{x}$ and time t

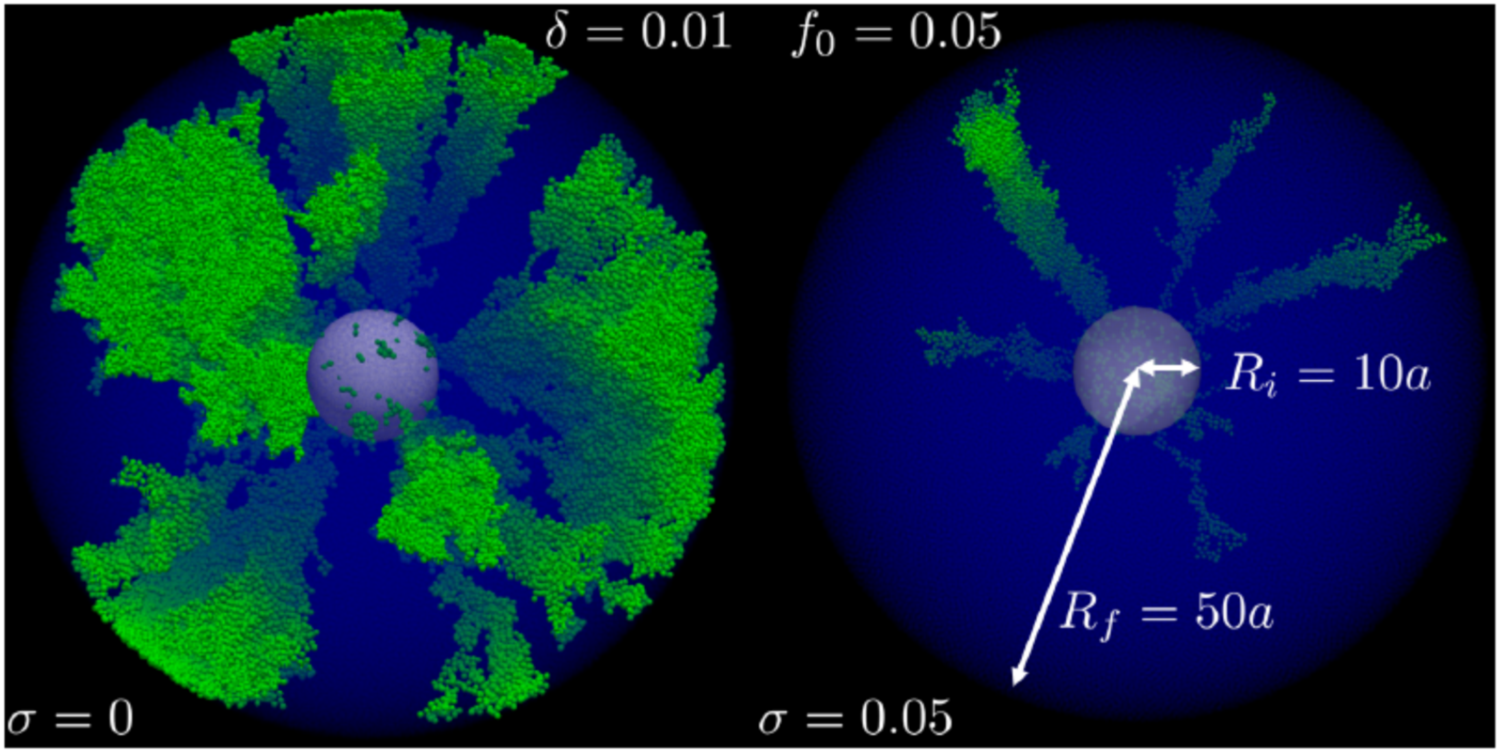


(Dynamics controlled by the foot of the wave, f << 1)

(Dynamics controlled further back, f> f*, Allee effect)

Nucleation in a growing spherical cluster

Application to prevascular tumors?



In a growing cluster of cells with inflating radius $R(t) = \alpha(t)R_0$ and $\alpha(t) = 1 + t/t^*$, the survival probability will be enhanced. One can see from the droplet dynamics ($\gamma = \sqrt{D_s\sigma}/12, c = \delta/12$):

$$E = 2\gamma\alpha(t)\pi\bar{r}_0 - c[\alpha(t)]^2\pi\bar{r}_0^2 \quad \Rightarrow \quad \bar{r}_0^* = \left[\int_0^\infty \frac{2\pi ct^* e^{-z}\,\mathrm{d}z}{z + 2\pi ct^*}\right] r_0^* \ll r_0^*$$

Pushed Genetic Waves and Antagonistic Interactions

Andrea

- *For pushed genetic waves, a "critical nucleus" is required to excite the wave to get it started (like nucleation theory)*
- *How can an excitable pushed wave from a gene drive be stopped? (They are fragile and can be stopped by obstacles….)*
- *Can we detect the existence of a critical nucleus with killer yeast or bacteria strains? (project with Andrea & Andrew)*

Andrew

Max Lavrentovich
Univ. of Tennessee

Thank you!

http://streetanatomy.com