The motion of hybrid zones (and how to stop them)

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Hybrid Zones

A hybrid zone is a narrow geographic region where two genetically distinct populations are found close together and hybridise to produce offspring of mixed ancestry.

They are maintained by a balance between selection and dispersal.

With thanks to Nick Barton and his group

A mathematical model

We focus on selection against heterozygosity

Individuals carry two copies of a gene that occurs as a or A.

Hardy-Weinberg proportions: $\overline{w} =$ proportion of a-alleles,

aa	aA	AA
$\overline{w}^2$	$2\overline{w}(1-\overline{w})$	$(1-\overline{w})^2$

Relative fitnesses:

aa	aA	AA
1	$1-s$	1

Reproduction

- Each heterozygote (aA) produces $(1-s)$ times as many germ cells (cells of same genotype) as a homozygote (aa or AA);
- Germ cells split into effectively infinite pool of gametes (containing just one copy of gene),
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$$\overline{w}^* = \frac{\left(\overline{w}^2 + \overline{w}(1-\overline{w})(1-s)\right)}{\left(\overline{w}^2 + 2\overline{w}(1-\overline{w})(1-s) + (1-\overline{w})^2\right)}$$

$$= \frac{\overline{w}^2 + \overline{w}(1-\overline{w})(1-s)}{1-2s\overline{w}(1-\overline{w})}$$

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Add dispersal:

$$\frac{\partial w}{\partial t} = \frac{m}{2}\Delta w + \alpha w(1-w)(2w-1).$$

Finite population effects? Population size N

- $2N$ gametes sampled at random from pool
- Fuse at random to produce offspring

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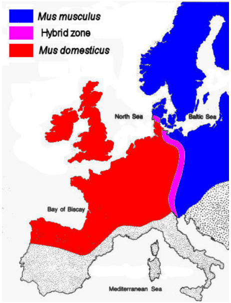
has no solution in dimensions $d \geq 2$, but can modify approach

Examples of hybrid zones

Maintained by selection?

$$\frac{\partial w}{\partial t} = \frac{m}{2}\Delta w + \alpha w(1-w)(2w-1)$$

plus noise



Width of zone

$$\approx \sqrt{\frac{2m}{\alpha}}$$

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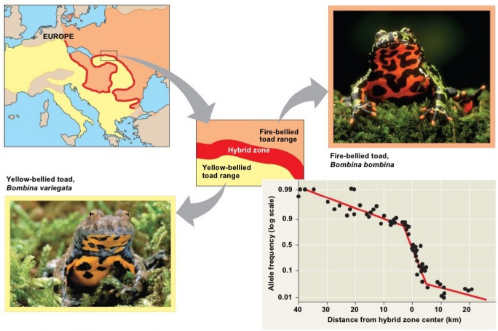
Maintained by selection?

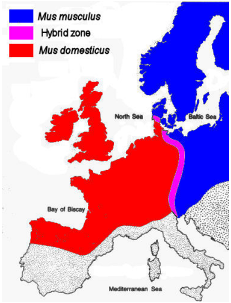
$$\frac{\partial w}{\partial t} = \frac{m}{2}\Delta w + \alpha w(1-w)(2w-1)$$

plus noise

or, eg changes in environment?

Fig. 24-13





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Zooming out

Applying a diffusive rescaling $t \mapsto \frac{t}{\varepsilon^2}$, $x \mapsto \frac{x}{\varepsilon}$, the Allen-Cahn equation becomes

$$\frac{\partial w}{\partial t} = \frac{m}{2}\Delta w + \frac{\alpha}{\varepsilon^2} w(1-w)(2w-1).$$

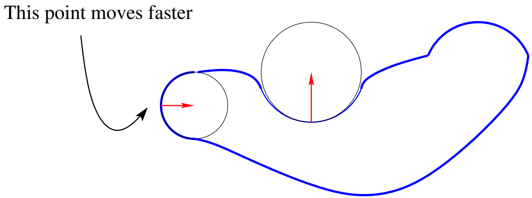
For convenience, set $m = 2$, $\alpha = 1$.

For sufficiently regular initial conditions, as $\varepsilon \to 0$, the solution converges to the indicator function of a region whose boundary evolves according to *curvature flow*.

(Mean) Curvature flow

- $\mathbf{\Gamma}_t : S^1 \to \mathbb{R}^2$ smooth embeddings;
- $\mathbf{n}_t(u)$ unit (inward) normal vector to $\mathbf{\Gamma}_t$ at u;
- $\kappa = \kappa_t(u)$ curvature of $\mathbf{\Gamma}_t$ at u.

$$\frac{\partial \mathbf{\Gamma}_t(u)}{\partial t} = \kappa_t(u)\mathbf{n}_t(u).$$ Defined up to fixed time T

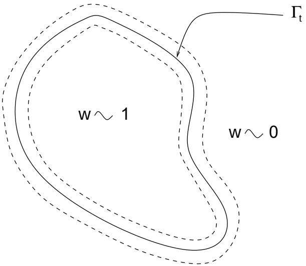


The Allen-Cahn equation and curvature flow

$d(x,t) =$ signed distance x to $\mathbf{\Gamma}_t$

$\mathbf{\Gamma}_0 = \{x \in \mathbb{R}^2 : w_0(x) = \frac{1}{2}\}$

$w_0 > \frac{1}{2}$ inside $\mathbf{\Gamma}$, $< \frac{1}{2}$ outside



$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-1).$$

Theorem (Chen 1992)
Fix $T^* \in (0,T)$. Let $k \in \mathbb{N}$. There exists $\varepsilon(k) > 0$, and $a(k), c(k) \in (0,\infty)$ such that for all $\varepsilon \in (0,\varepsilon(k))$ and t satisfying $a\varepsilon^2 |\log \varepsilon| \leq t \leq T^*$,

1. for x such that $d(x,t) \geq c\varepsilon |\log \varepsilon|$, we have $w(t,x) \geq 1 - \varepsilon^k$;
2. for x such that $d(x,t) \leq -c\varepsilon |\log \varepsilon|$, we have $w(t,x) \leq \varepsilon^k$.

A probabilistic proof (E. Freeman, Penington, 2017)

Ternary branching Brownian motion

- Individual lifetime $\mathtt{Exp}(1/\varepsilon^2)$;
- During lifetime follows Brownian motion;
- Replaced by three offspring.

Majority voting in (Historical) BBM

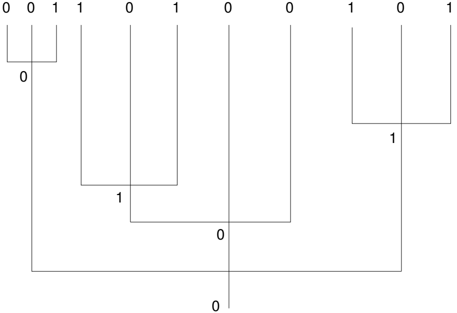
Adaptation of idea of del Masi, Ferrari & Lebowitz (1986)
$\boldsymbol{W}(t)$ = historical ternary BBM.

For a fixed function $w_0 : \mathbb{R}^2 \to [0, 1]$, define a voting procedure on $\boldsymbol{W}(t)$ as follows.

1. Each leaf, independently, votes 1 with probability $w_0(W_i(t))$ and otherwise votes 0.
2. At each branch point the vote of the parent particle is the majority vote of the votes of its three children.

This defines an iterative voting procedure, which runs inwards from the leaves of $\boldsymbol{W}(t)$ to the root.
Define $\mathbb{V}_{w_0}(\boldsymbol{W}(t))$ to be the vote associated to the root.

Majority voting and the Allen-Cahn equation



$\boldsymbol{W}(t) =$ historical BBM, branching rate $\frac{1}{\varepsilon^2}$; $w_0 : \mathbb{R}^2 \to [0,1]$.

$$w(t,x) = \mathbb{P}_x^{\varepsilon}\left[\mathbb{V}_{w_0}(\boldsymbol{W}(t)) = 1\right]$$

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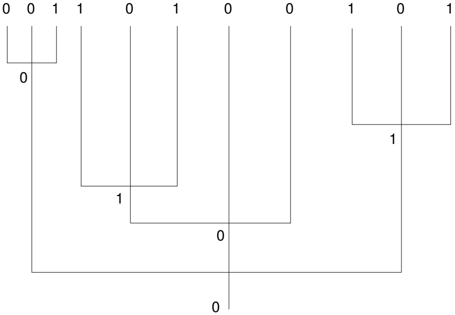

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Note that if probability of voting 1 is w, the probability that the majority of 3 independent votes is 1 is
$w^3 + 3w^2(1-w) = w(1-w)(2w-1) + w$.

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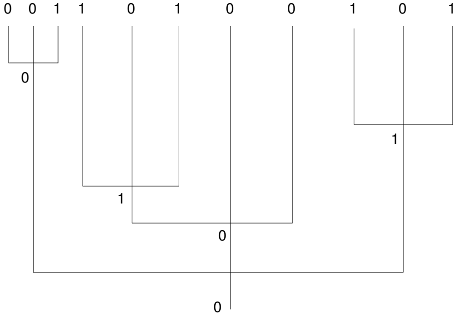

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$$w(t,x) = \mathbb{P}_x^{\varepsilon}\left[\mathbb{V}_{w_0}(\boldsymbol{W}(t)) = 1\right]$$

solves

$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-1), \quad w(0,x) = w_0(x).$$

Probabilistic proof of Chen's result

Representation reduces result to

1. for x with $d(x,t) \geq c\varepsilon|\log\varepsilon|$, $\mathbb{P}^{\varepsilon}_{x}\left[\mathbb{V}_{w_0}(\boldsymbol{W}(t)) = 1\right] \geq 1 - \varepsilon^{k}$;
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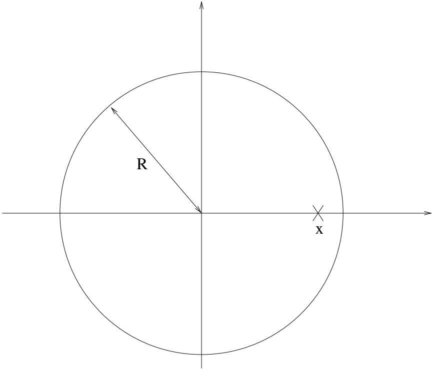
Two mechanisms:

- Majority voting amplifies voting bias;
  $(p > \frac{1}{2} \implies p^3 + 3p^2(1-p) > p;$
  $p < \frac{1}{2} \implies p^3 + 3p^2(1-p) < p)$
- for two-dimensional BM W and one-dimensional BM B, couple so that $d(W_s, t-s) \approx B_s$ when W_s is close to $\mathbf{\Gamma}_{t-s}$ (uses regularity assumptions on initial condition)

Some heuristics

Small $\varepsilon \implies$ many rounds of majority voting $\rightsquigarrow$ generation of an interface.

Suppose there is already a sharp (circular) interface.



For the point x,

$\mathbb{P}_x[W_{\delta t}$ outside ball$] = 1/2$

$\mathbb{P}_x[B_{\delta t} + \frac{1}{R}\delta t > R] = 1/2$

$x = R - \frac{1}{R}\delta t$.

c.f. Merriman-Bence-Osher algorithm

What if homozygotes not equally fit?

Relative fitnesses:

aa	aA	AA
$1+\gamma s$	$1-s$	1

Equation becomes

$$\frac{\partial w}{\partial t} = \Delta w + sw(1-w)((2+\gamma)w - 1).$$

Take $\gamma = \mathcal{O}(\varepsilon)$ and rescale:

$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w - (1-\nu\varepsilon)).$$

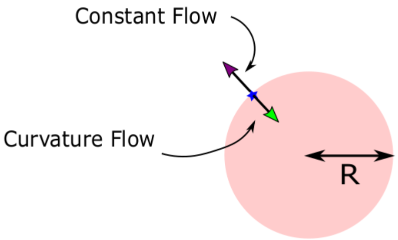
Sensitivity to asymmetry (Gooding, 2018)

$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-(1-\nu\varepsilon)).$$

Limit a mixture of curvature flow and 'constant flow':

$$\frac{\partial \mathbf{\Gamma}_t(u)}{\partial t} = \big(-\nu + \kappa_t(u)\big)\mathbf{n}_t(u).$$

Defined up to fixed time T



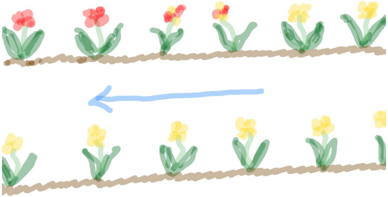
Invasions

$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-(1-\nu\varepsilon)).$$

In $d = 1$, travelling wave solution (pushed wave)

$$w(x,t) = \left(1 + \exp\left(-\frac{x+\nu t}{\varepsilon}\right)\right)^{-1}$$

wave speed $-\nu$, connects 0 at $-\infty$ to 1 at ∞



Blocking (E., Gooding, Letter, 2022)

Consider a domain $\Omega \subseteq \mathbb{R}^2$ (and containing the x-axis, say)

When do we have invasion?

$$\frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-(1-\nu\varepsilon)), \quad w(0,x) = \mathbf{1}_{x_1 \geq 0}.$$

Theorem (H. Berestycki et al., 2016) (paraphrased)
Depending on the geometry of the domain:

1. complete invasion;
2. partial propagation;
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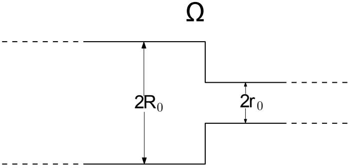
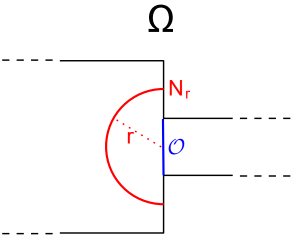


A more precise statement

$$\begin{cases} \frac{\partial w}{\partial t} = \Delta w + \frac{1}{\varepsilon^2} w(1-w)(2w-(1-\nu\varepsilon)); \\ \frac{\partial w}{\partial n} = 0, \qquad w(x,0) = 1_{x_1 \geq 0}; \end{cases}$$



Theorem

Suppose $r_0 < r < \frac{\mathrm{d}-1}{\nu} \wedge R_0$. Let $k \in \mathbb{N}$. Then for $\varepsilon \in (0, \hat{\varepsilon}(k))$

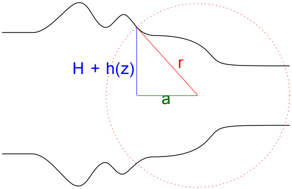
$$x \in \{x = (x_1, \ldots, x_d) : x_1 < -r - M(k)\varepsilon|\log(\varepsilon)|\} \implies w(x,t) \leq \varepsilon^k.$$

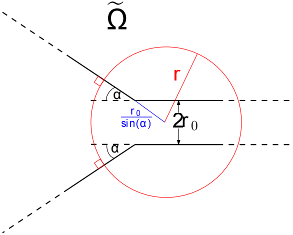
Other domains

E.g. cylindrical domain:

$$\Omega = \left\{ (x_1, x'), x_1 \in \mathbb{R}, x' \in \mathbb{R}^{d-1}, \|x'\| \leq H + h(-x_1) \right\}$$

Key is coupling around a portion of a spherical shell





If $r_0 \nu < (d - 1) \sin \alpha$ wave blocked for small ε.

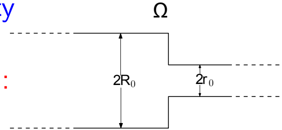
Effect of noise

With space, morally,

$$dw_t = \Big(\frac{m}{2}\Delta w + \alpha w(1-w)(2w-1)\Big)dt + \sqrt{\beta w(1-w)}W(dt,dx)$$

β inversely proportional to population density

Two dimensions, narrow isthmus $(r_0 < 1/\nu)$:



- If genetic drift is weak (population density high), the spread of the favoured type is blocked;
- If genetic drift is strong (population density low), the favoured population spreads across the whole domain, *but we have coexistence*.

Proof uses voting on a branching and *coalescing* system

Conclusion

- Space matters
- The *shape of the domain* matters
- Noise matters

Where next?

With energy, could extend this approach to traits determined by the types at a (small) number of genetic loci

- What about traits determined by accumulation of small effects at very large number of loci (plus some environmental noise)?

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Even loci on different chromosomes are constrained by a pedigree; the pedigree mediates the effect of Mendelian inheritance

Noise matters: need a tractable mathematical model that can keep track of both trait values and ‘pedigree relationships’ between individuals