

The KPZ universality conjecture: Old ideas and new applications

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- An introduction to KPZ scaling theory
- KPZ behavior in microbial colonies
- Surface growth & spatial evolution models

YITP Workshop “Interface fluctuations and KPZ universality class”

Kyoto, August 20, 2014

Prehistory

- Diffusion-limited aggregation Witten & Sander 1981
- Active zone of Eden clusters Plischke & Rácz 1984
- Scaling form of the surface width Family & Vicsek 1985
- Stochastic continuum theory Kardar, Parisi, Zhang 1986
- Precursors:
 - Stochastic Burgers equation Forster, Nelson, Stephen 1977
 - Excess noise in driven diffusive systems van Beijeren, Kutner, Spohn 1985
- Key insight: Growth processes governed by two universal scaling exponents α, z with $\alpha = 1/2, z = 3/2$ in 1+1 dimensions
- Scaling relation $\alpha + z = 2$ in all dimensions JK 1987

The link to growth models

The one-dimensional KPZ equation

$$\frac{\partial h}{\partial t} = v\nabla^2 h + \frac{\lambda}{2}(\nabla h)^2 + \eta, \quad \langle \eta(x, t)\eta(x', t') \rangle = D\delta(x - x')\delta(t - t')$$

can be connected **quantitatively** to discrete growth models through

- the stationary height fluctuations:

Huse, Henley, Fisher 1985

$$\lim_{t \rightarrow \infty} \langle [h(x+r, t) - h(x, t)]^2 \rangle = A|r| \quad \text{with} \quad A = \frac{D}{2v}$$

- the inclination-dependent growth rate: $\lambda = v''(u)$

JK, H. Spohn 1990

- The finite size correction to the growth rate:

JK, P. Meakin 1990

$$v(L = \infty) - v(L) = \frac{\lambda A}{2L} + \mathcal{O}(1/L^2)$$

KPZ scaling theory

- Use the KPZ equation to identify the dimensions of the two macroscopic parameters A and λ :

$$[A] = \frac{[h]^2}{[x]}, \quad [\lambda] = \frac{[x]^2}{[h][t]}$$

- Thus refined universality is expected to hold in terms of the non-dimensional variables

$$\tilde{h} = \frac{h}{(A^2|\lambda|t)^{1/3}}, \quad \tilde{x} = \frac{x}{(A\lambda^2t^2)^{1/3}}$$

- In modern notation

Prähofer & Spohn 2000

$$h(x,t) = vt + \text{sgn}(\lambda) \left(\frac{1}{2}A^2|\lambda|t \right)^{1/3} \chi$$

where χ is a universal random variable

Early numerical amplitude estimates

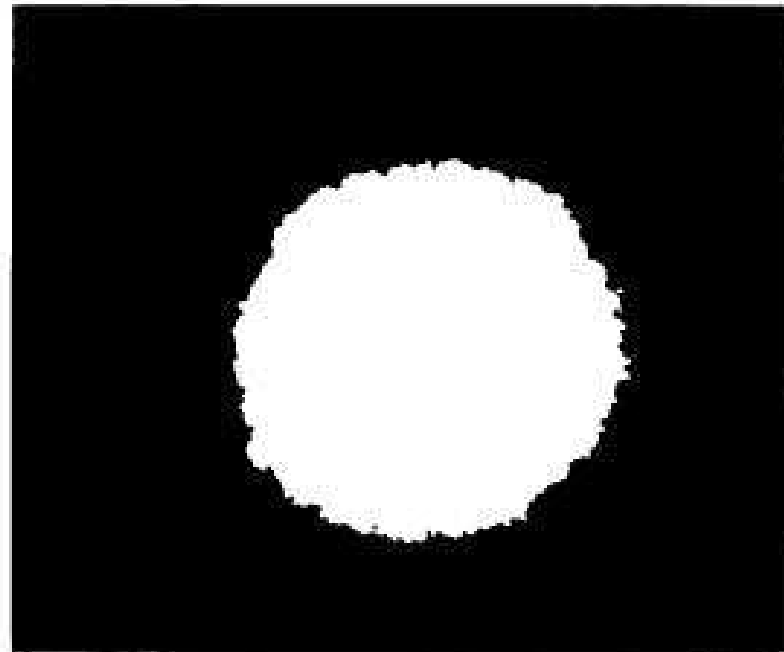
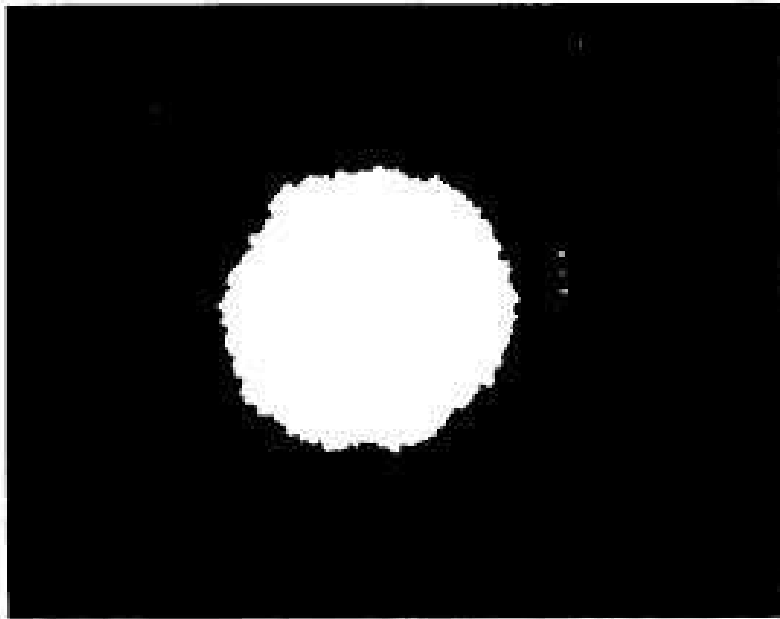
JK, P. Meakin, T. Halpin-Healy 1992

class	mean	variance	skewness	kurtosis
flat (growth)	-0.73 ± 0.05	0.64 ± 0.02	0.28 ± 0.04	0.12 ± 0.01
flat (DPRM)	-0.68 ± 0.05	0.63 ± 0.09	0.296 ± 0.028	
flat (KMB*)			0.29 ± 0.02	≈ 0.16
TW GOE	-0.76007	0.63805	0.2935	0.1652
stationary	0	1.130 ± 0.005	0.331 ± 0.007	
F_0	0	1.15039	0.35941	

*Kim, Moore, Bray 1991

- The existence of a third ('curved/point-to-point') class with distinct amplitudes was noticed in 1992, but no numerical estimates were reported
- From the KPZ picture it is evident that $\langle \chi \rangle < 0$ for the non-stationary classes

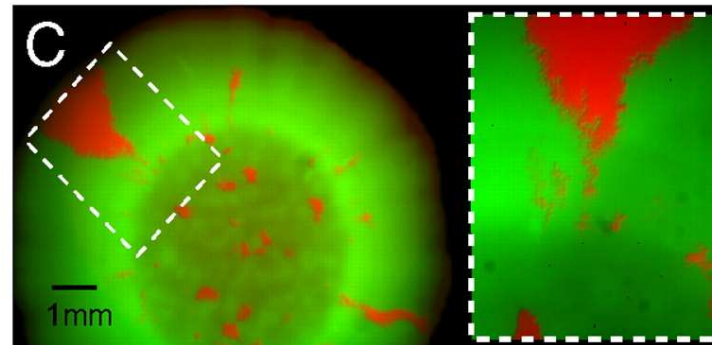
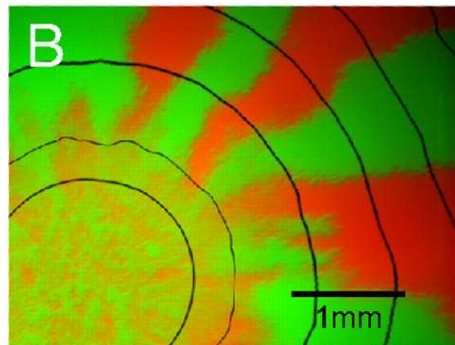
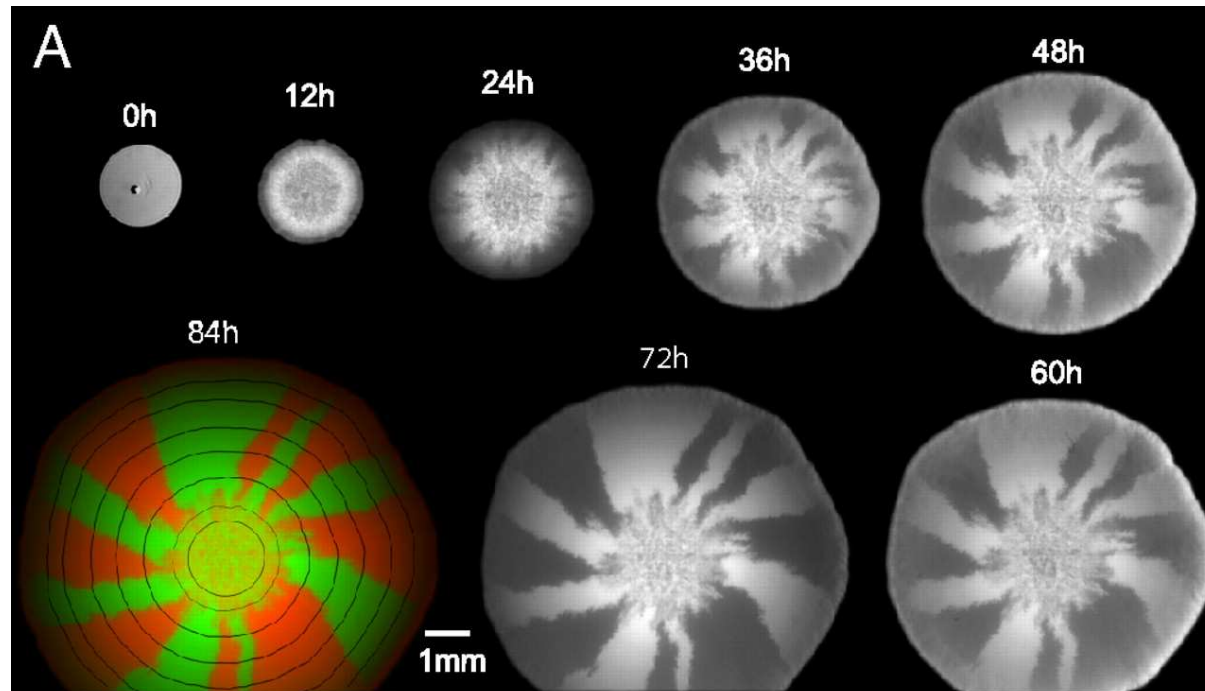
KPZ behavior in microbial colonies



Eden 1961

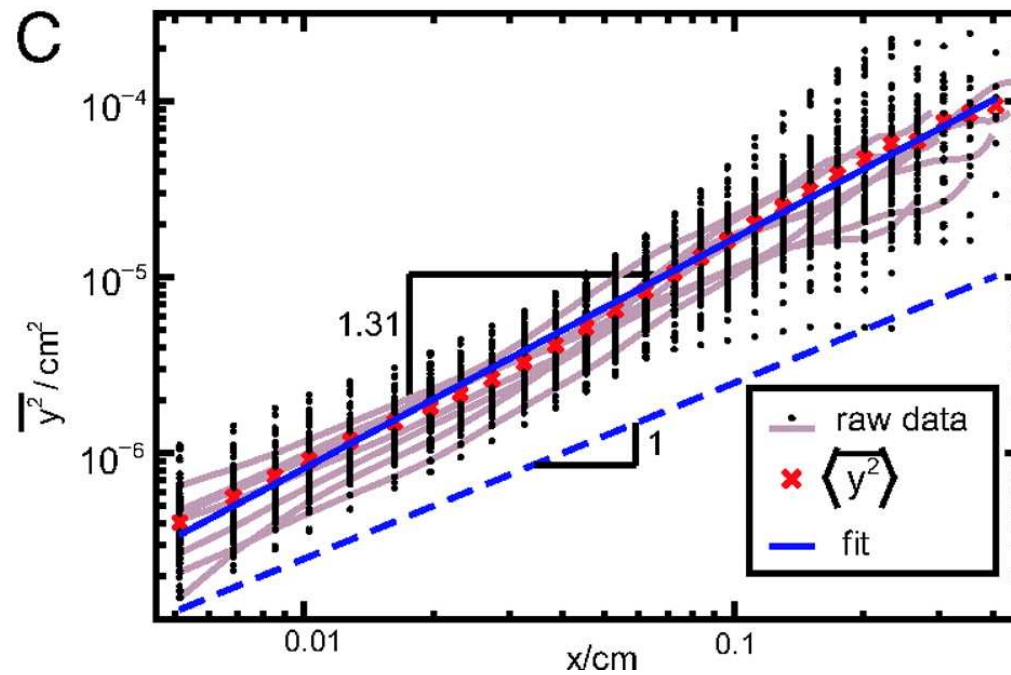
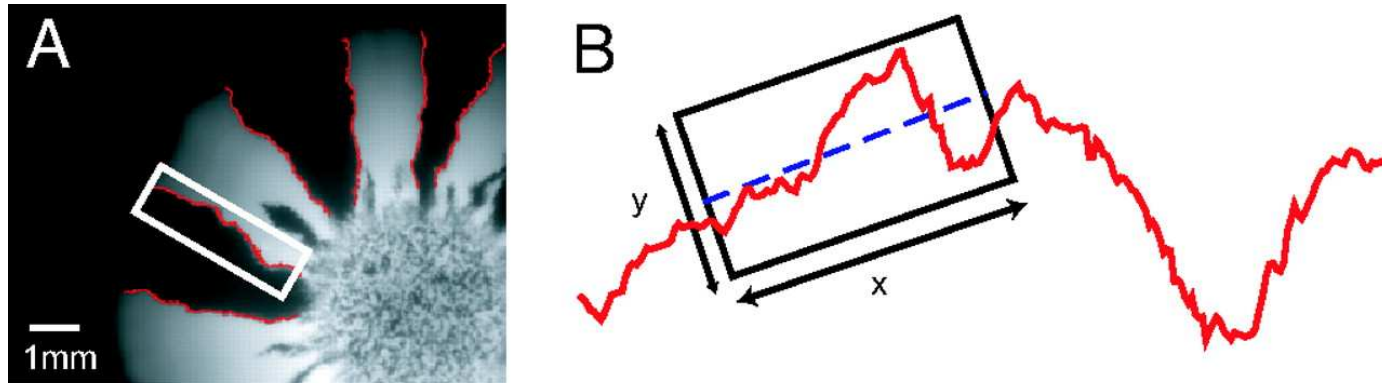
Genetic segregation in growing bacterial colonies

Hallatschek et al., PNAS 2007



Sector boundaries display superdiffusive KPZ fluctuations

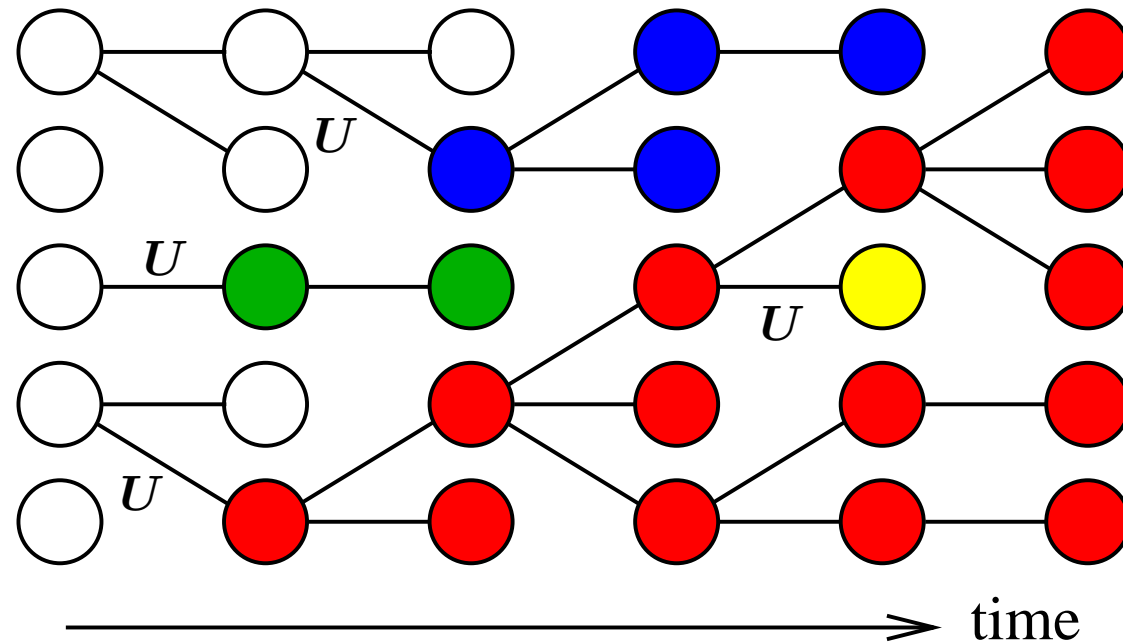
Hallatschek et al., PNAS 2007



Basic concepts of population genetics

S.-C. Park, D. Simon, JK, J. Stat. Phys. 138:381 (2010)

Wright-Fisher model for asexual populations



- N individuals, discrete generations
- Individuals have **types** which can change through mutations (rate U)
- An individual is chosen as parent with a probability proportional to its **fitness**
- No spatial structure (“well-mixed” population)

Selection

- K types, n_i individuals of type i , $\sum_{i=1}^K n_i = N$, type i has fitness w_i
- Neglecting mutations and fluctuations (“genetic drift”) the genetic structure of the population evolves according to

$$n_i(t+1) = \frac{w_i}{\langle w \rangle(t)} n_i(t), \quad \langle w \rangle(t) = \frac{1}{N} \sum_i w_i n_i(t)$$

- **Continuous time dynamics:** generation time Δt , $w_i = e^{\Delta t f_i}$

$$\Rightarrow \frac{dn_i}{dt} = (f_i - \langle f \rangle) n_i \text{ for } \Delta t \rightarrow 0$$

$$\Rightarrow \frac{d}{dt} \langle f \rangle = \frac{1}{N} \sum_{i=1}^K f_i \dot{n}_i = \langle f^2 \rangle - \langle f \rangle^2 \geq 0$$

“Fisher’s fundamental theorem”

- For $t \rightarrow \infty$ the best type wins and $\langle f^2 \rangle - \langle f \rangle^2 \rightarrow 0$

Fixation

- $U = 0$: When a single mutant of fitness w' is introduced into a homogeneous population of fitness w , the outcome for $t \rightarrow \infty$ is either fixation (**all w'**) or loss of the mutation (**all w**)
- Fixation probability for the Wright-Fisher model Kimura 1962

$$\pi_N(s) \approx \frac{1 - e^{-2s}}{1 - e^{-2Ns}}, \quad s = \frac{w'}{w} - 1 \quad \text{selection coefficient}$$

- Under **strong selection**: ($N|s| \gg 1$) deleterious mutations ($s < 0$) cannot fix, while beneficial mutations ($s > 0$) fix with probability

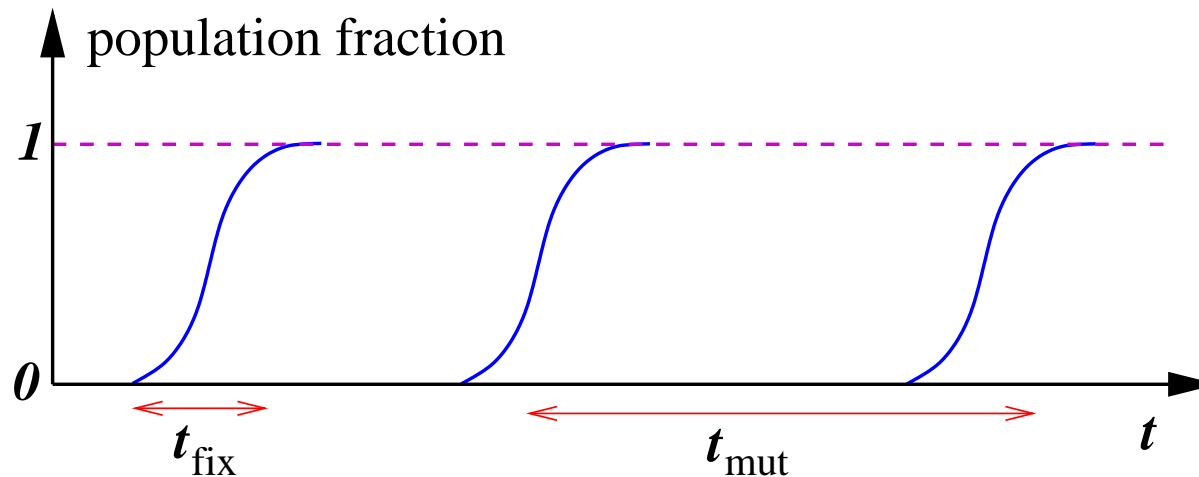
$$\pi(s) = 1 - e^{-2s} \approx 2s, \quad s \ll 1$$

- Mean time to fixation of a beneficial mutation:

$$t_{\text{fix}} \approx \frac{2 \ln N}{s}$$

Regimes of evolutionary dynamics

- Beneficial mutations with selection coefficient $s_b > 0$ occur in the population at rate U_b per individual and generation
- Mutations are strongly beneficial in the sense of $Ns_b \gg 1$ but weakly beneficial in absolute terms ($s_b \ll 1$)
- A given mutation survives stochastic noise with probability $\pi_\infty(s_b) \approx 2s_b$
 \Rightarrow time between **established** mutations is $t_{\text{mut}} = (2s_b U_b N)^{-1}$

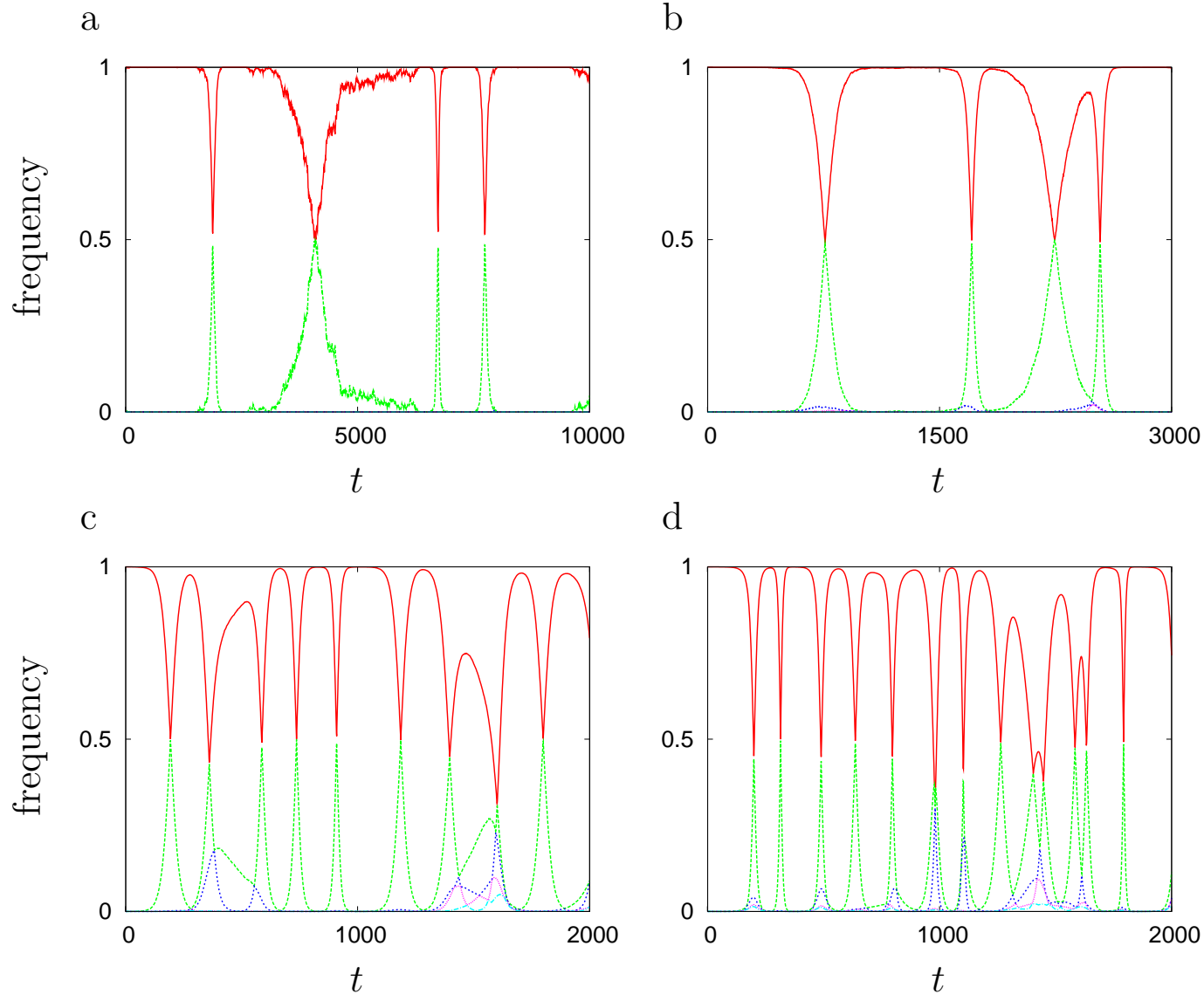


Periodic selection: $t_{\text{fix}} \ll t_{\text{mut}}$

Clonal interference: $t_{\text{fix}} \gg t_{\text{mut}}$

Onset of clonal interference

S.-C. Park, D. Simon, JK 2010

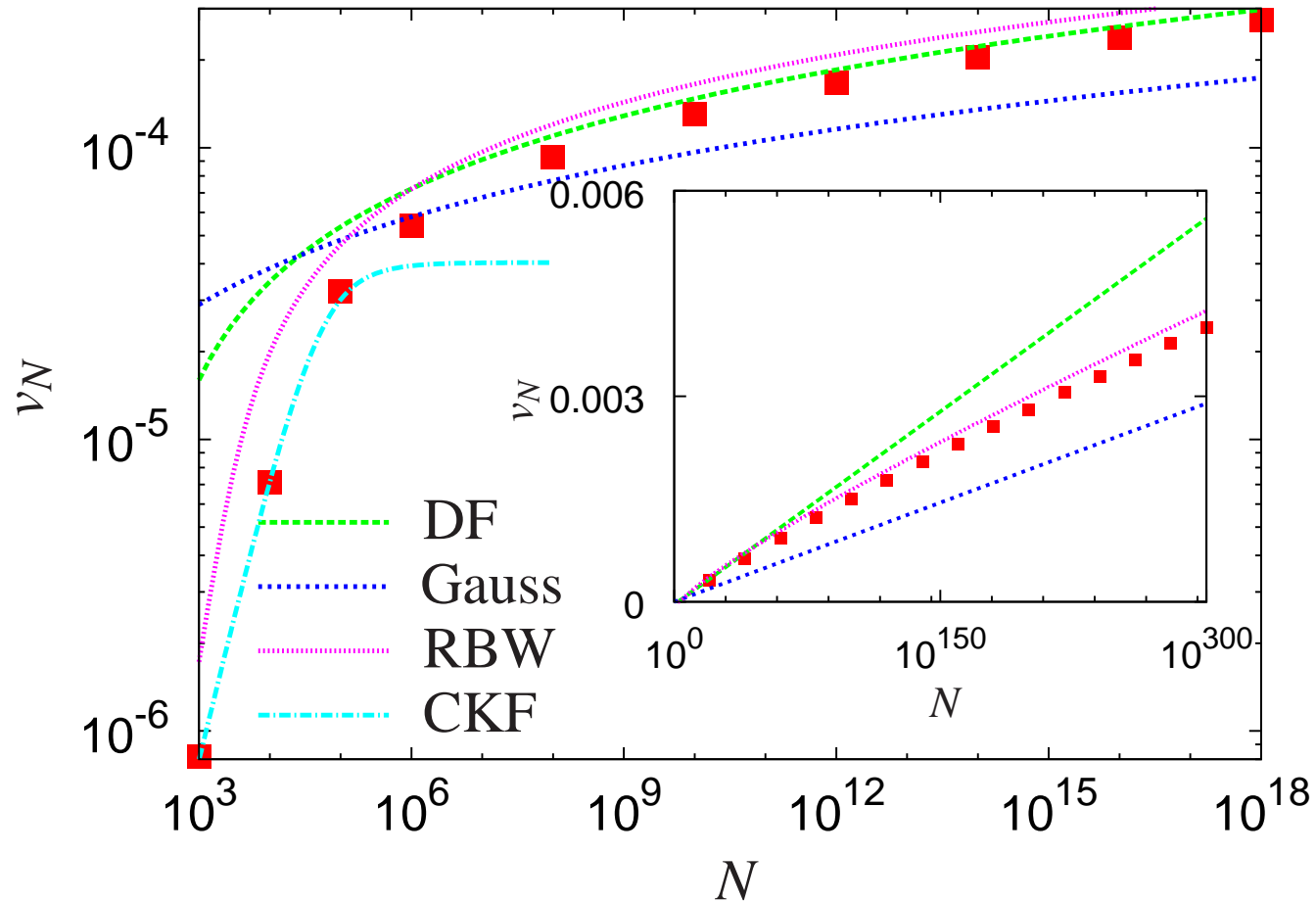


$$s_b = 0.02, U_b = 10^{-6}$$

$$N = 10^4, 10^5, 10^6, 10^7$$

Speed of evolution as a function of population size

S.-C. Park, D. Simon, JK 2010



● periodic selection: $v_N \sim N$

● clonal interference: $v_N \sim \ln N$

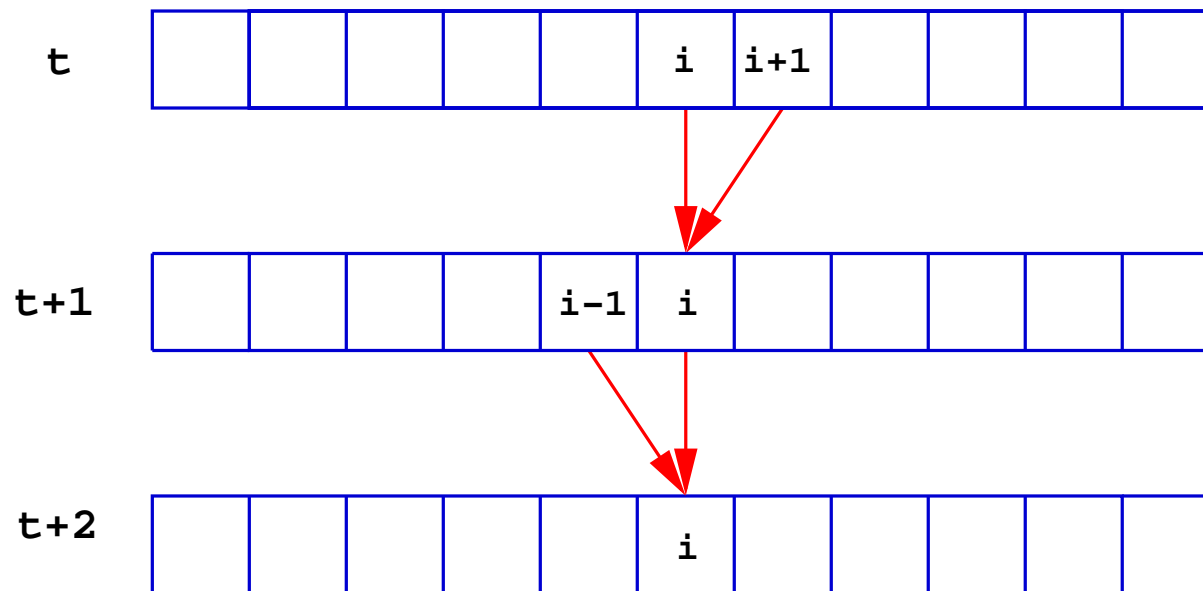
Surface growth & spatial evolution

with Jakub Otwinowski

arXiv:1302.4326, to appear in Physical Biology

Wright-Fisher model for spatial populations

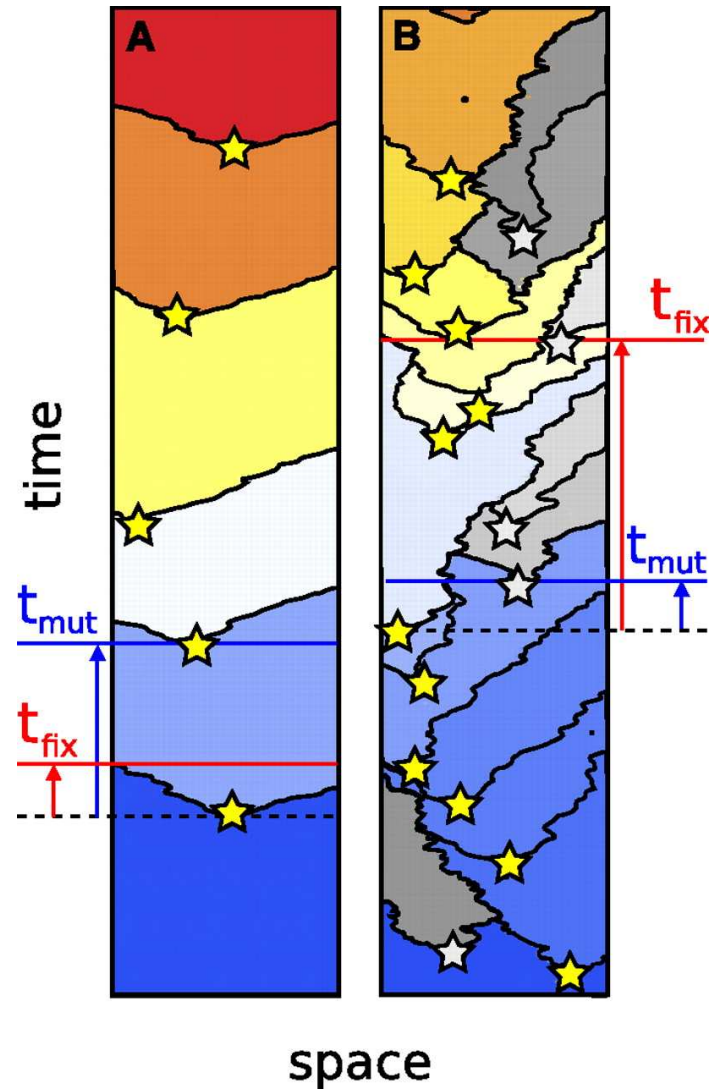
- Natural populations usually live in a spatial habitat and reproduce and compete **locally**
- Implementation on a d -dimensional lattice of length L with $N \sim L^d$:
(here $d = 1$)
J. Otwinowski, S. Boettcher, PRE 84:011925 (2011)



- Mutant clones spread **linearly** rather than exponentially

Clonal interference in spatial populations

E.A. Martens, O. Hallatschek, Genetics 189:1049 (2011)



Clonal interference in spatial populations

E.A. Martens, O. Hallatschek, Genetics 189:1049 (2011)

- Fixation probability is the same as in the well-mixed case Maruyama 1974

$$\Rightarrow t_{\text{mut}} = \frac{1}{2s_b U_b N} = \frac{1}{2s_b U_b L^d}$$

- Boundaries of mutant clones spread at speed $\sim s_b \Rightarrow t_{\text{fix}} \sim L/s_b$
- Clonal interference sets in above the **interference length** $L_c \sim U_b^{-1/(d+1)}$
- For $L \ll L_c$ adaptation occurs by periodic selection and the speed of evolution is $V \sim s_b/t_{\text{mut}} \sim s_b^2 U_b N$ as before
- What happens for $L \gg L_c$?

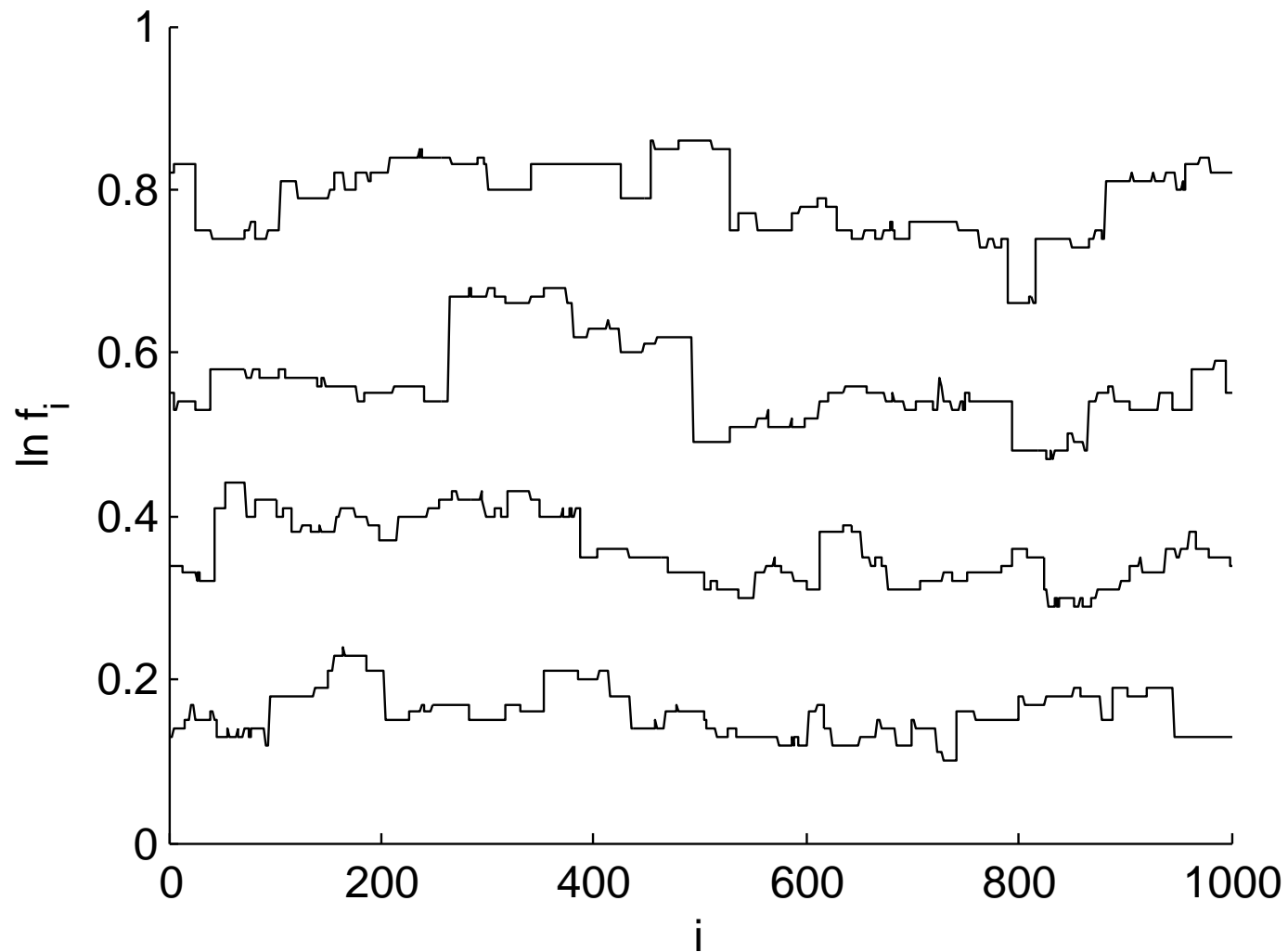
Analogy to polynuclear growth

- In the **polynuclear growth model (PNG)** crystal layers of unit height nucleate at random positions at rate Γ and the nuclei grow laterally at speed c
- For sample sizes $L < L_c \sim (c/\Gamma)^{1/(d+1)}$ growth occurs layer-by-layer and the growth rate is $\sim \Gamma L^d$
- Exact solution of the one-dimensional model shows that the growth rate saturates at $V_\infty \sim \sqrt{c\Gamma}$ for $L \gg L_c$ Goldenfeld 1984
- For general d dimensional analysis shows that $V_\infty \sim (c^d \Gamma)^{1/(d+1)}$ van Saarloos & Gilmer 1986
- At least for large selection coefficients ($s_b \approx 1$) the spatial Wright-Fisher model is equivalent to a PNG model with “surface height“ $\ln(w)$, nucleation rate $\sim s_b U_b$ and spreading velocity $\sim s_b$

$$\Rightarrow V_\infty \sim s_b^2 U_b^{1/(d+1)} \text{ independent of } L$$

Evolution of fitness/height profiles

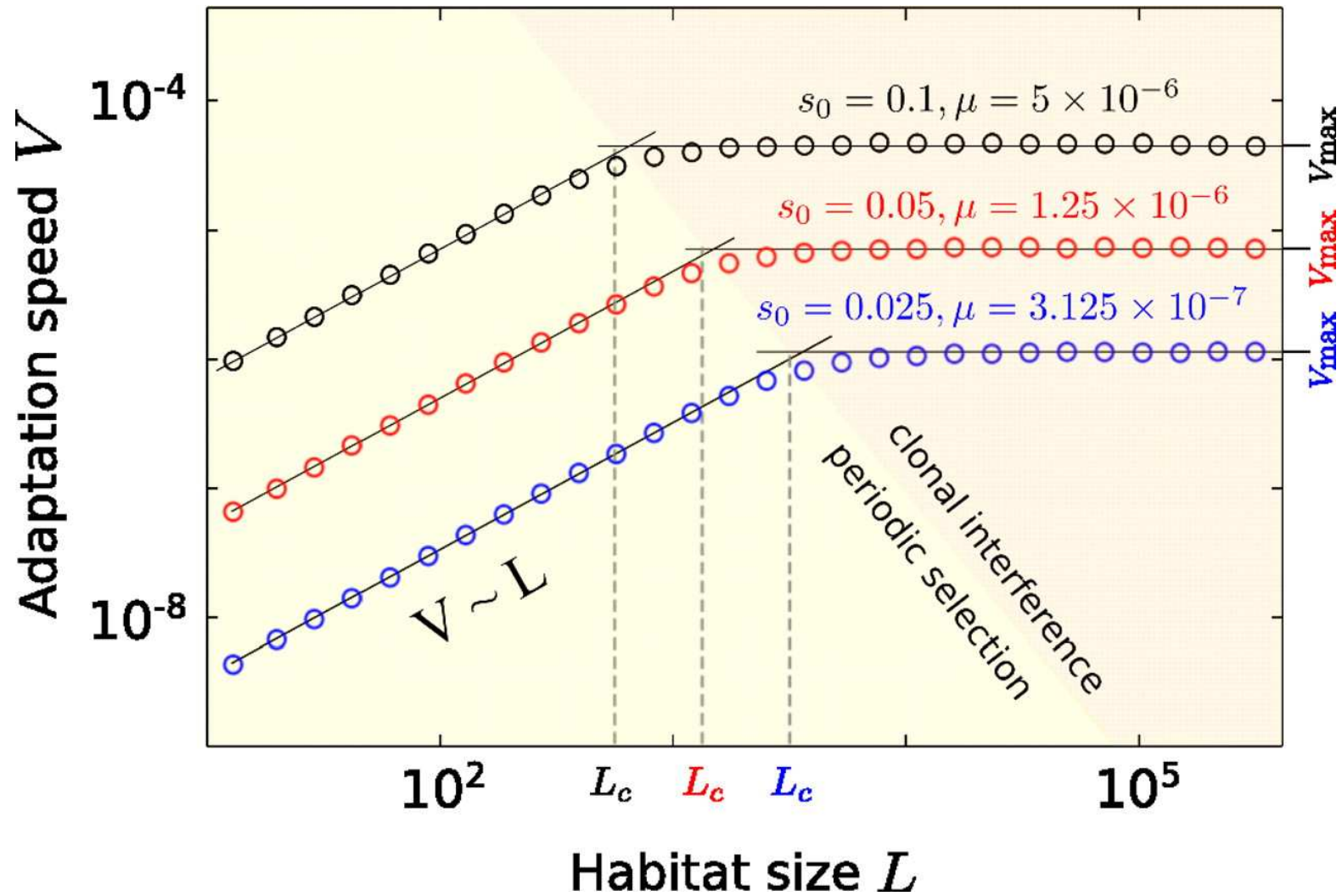
J. Otwinowski, S. Boettcher, PRE 84:011925 (2011)



$$s_b = 0.01, U_b = 0.001 \Rightarrow L_c \approx 30$$

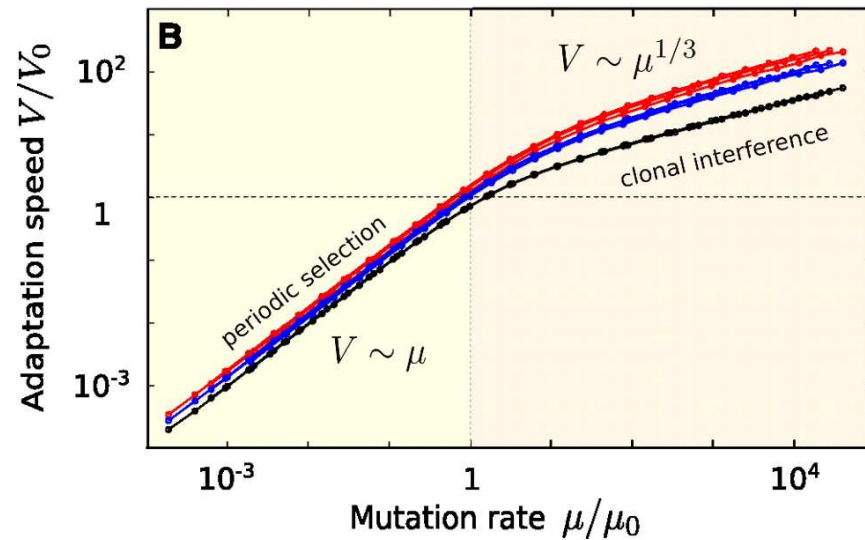
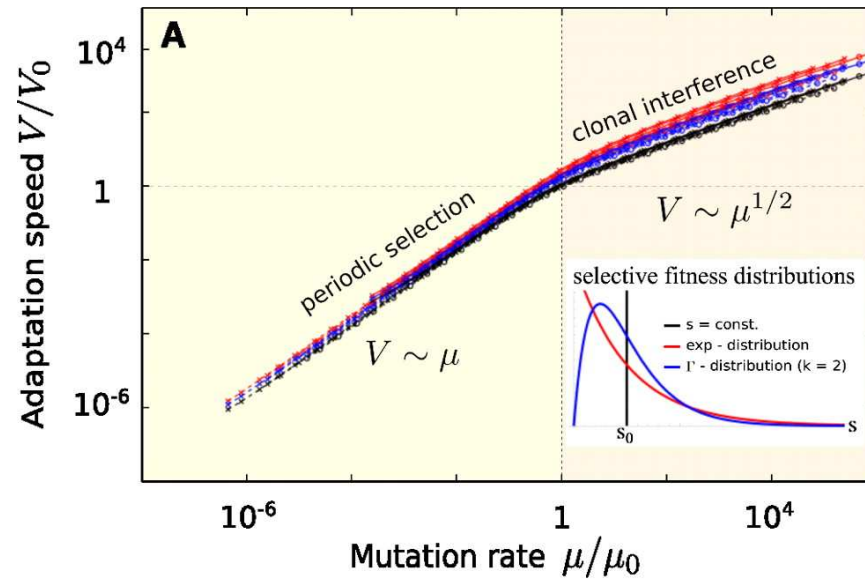
Speed of evolution in linear habitats ($d = 1$)

E.A. Martens, O. Hallatschek, Genetics 189:1049 (2011)



Speed of evolution vs. mutation rate

E.A. Martens, O. Hallatschek, Genetics 189:1049 (2011)



KPZ universality of fitness fluctuations?

- The PNG model is a prime representative of the KPZ universality class

Krug & Spohn 1989

- KPZ theory predicts that the fitness variance in one dimension grows as $\sigma^2 \sim t^{2/3}$ for times $t \ll t_x \sim L^{3/2}$ and saturates at $\sigma^2 \sim L$ for times $t \gg t_x$

- In contrast, the speed of adaptation $V = V_\infty = \mathcal{O}(1)$ for large L , in violation of Fisher's fundamental theorem $V \sim \sigma^2$

- Boundaries of competing clones move superdiffusively as $t^{2/3}$, which implies that the fixation time of mutations in the clonal interference regime is $\sim t_x \sim L^{3/2}$

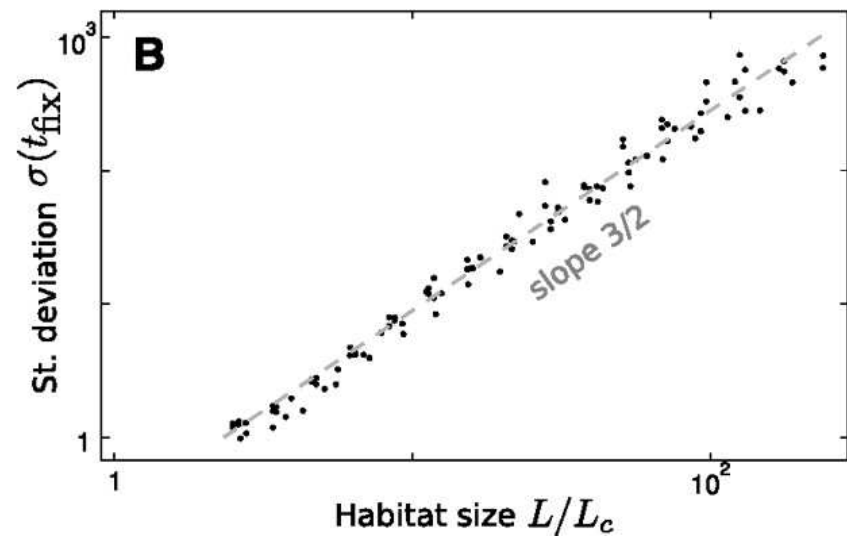
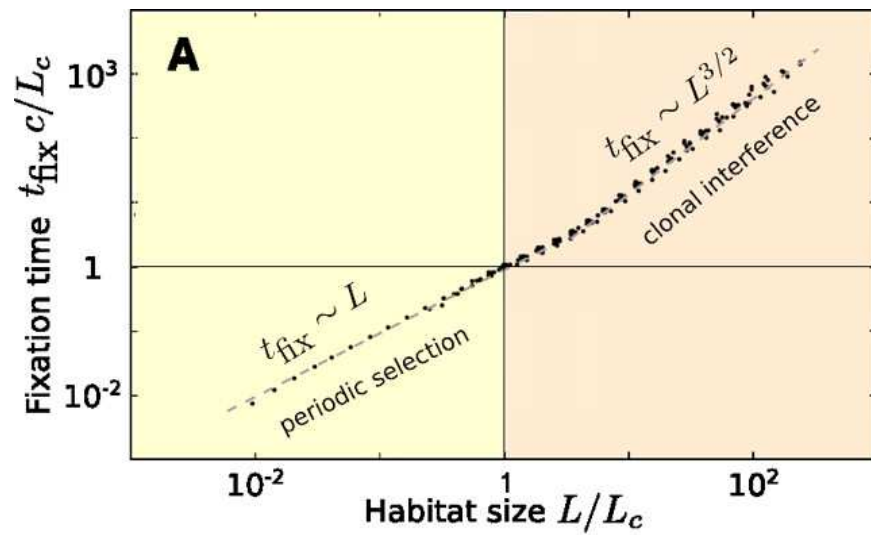
Martens & Hallatschek 2011

- Expect: Fitness fluctuations governed by geometry-dependent Tracy-Widom (TW) distributions

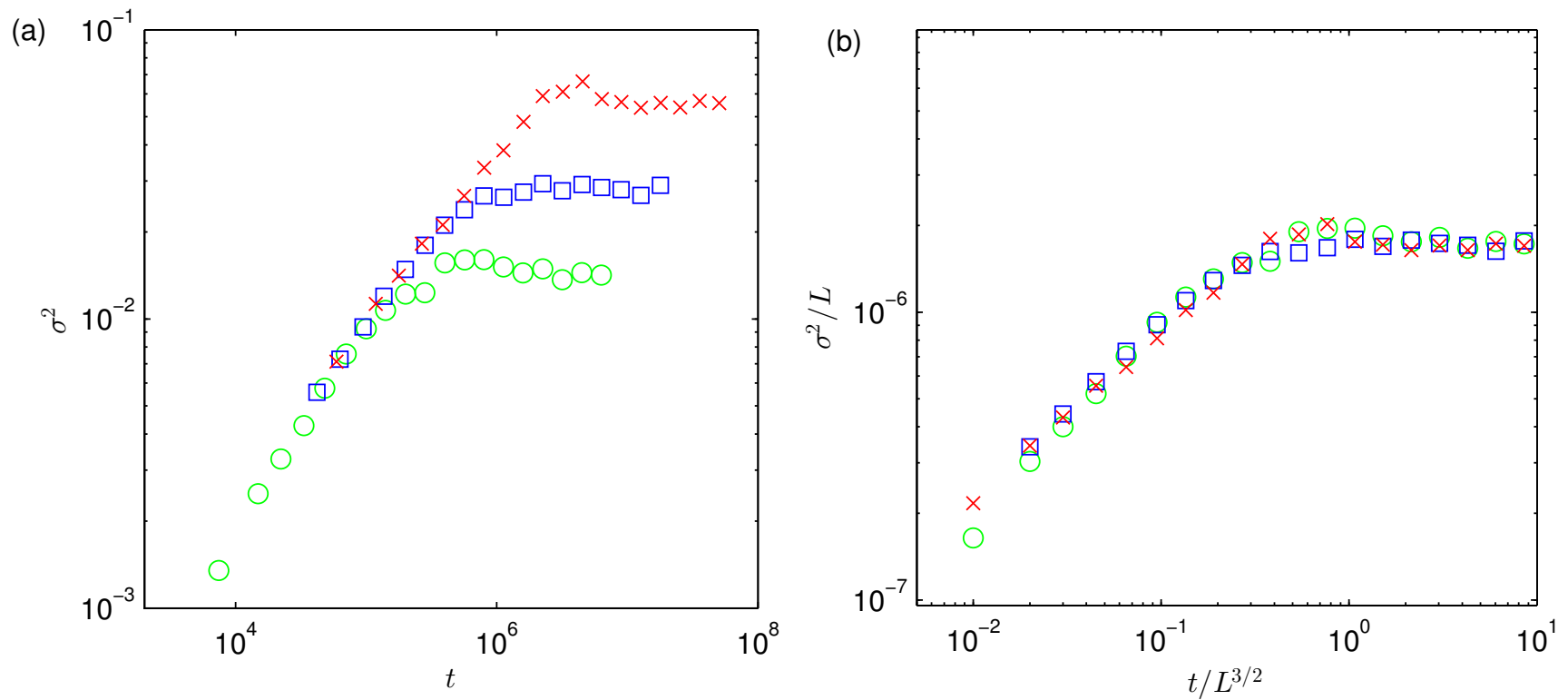
Prähofer & Spohn 2000

Fixation times in linear habitats

E.A. Martens, O. Hallatschek, Genetics 189:1049 (2011)

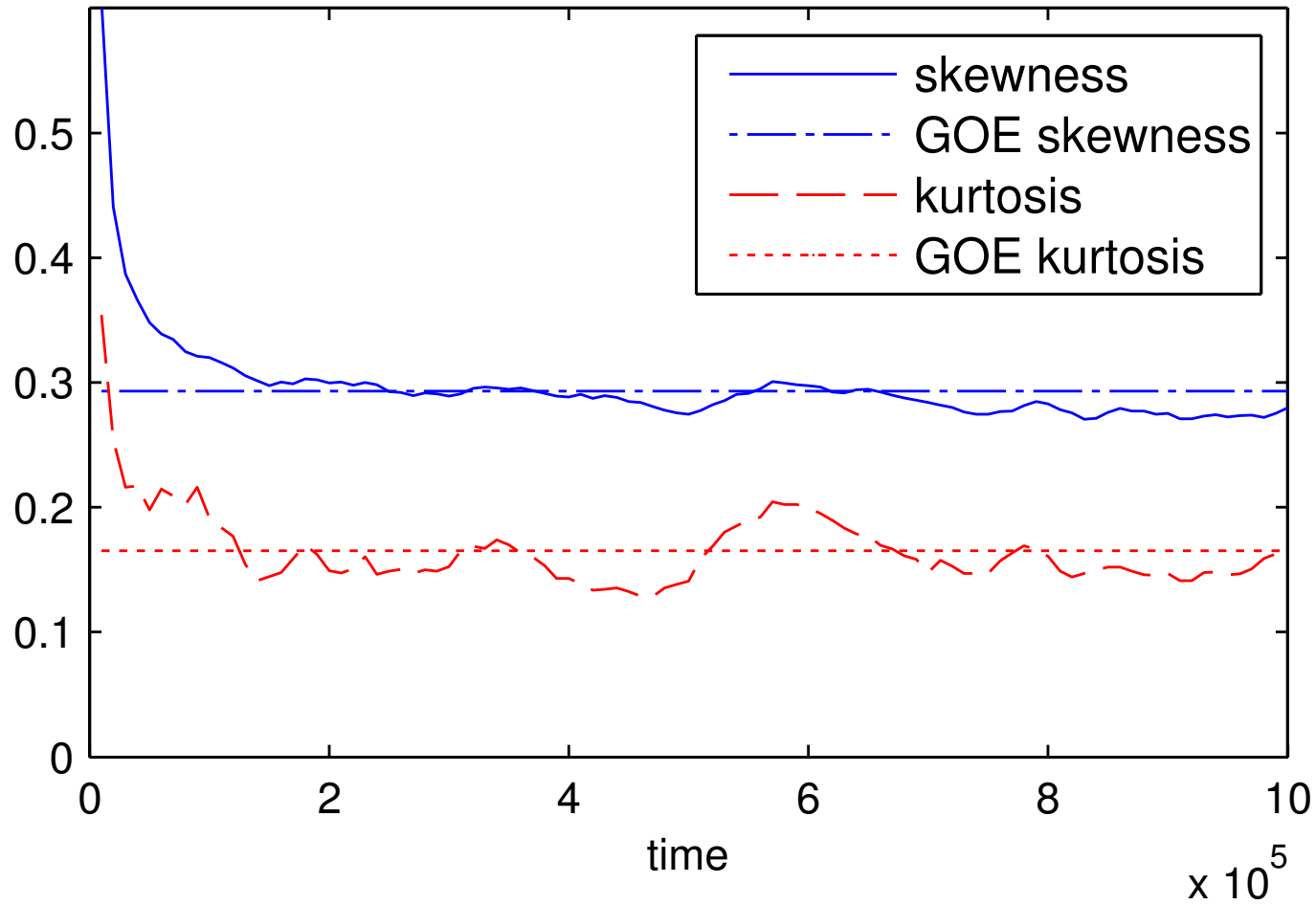


KPZ scaling of the fitness variance



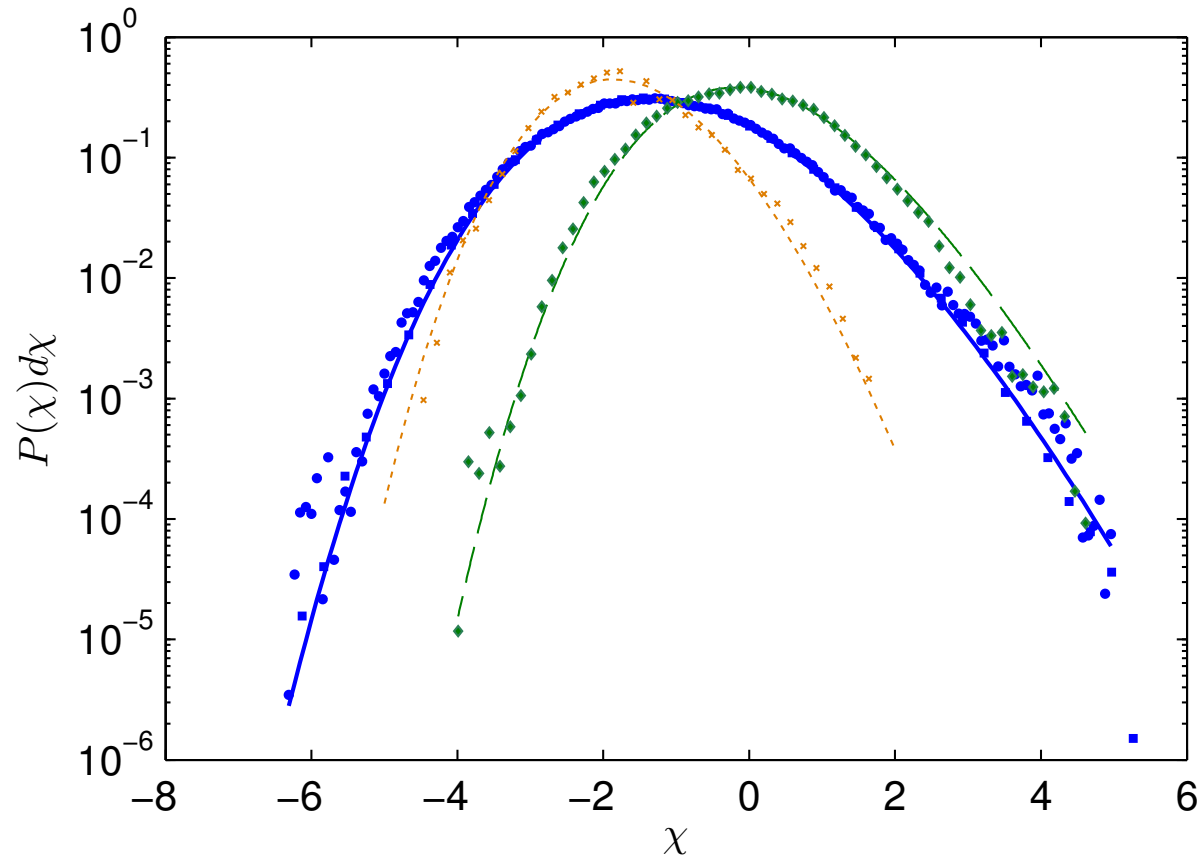
$$s_b = 0.05, U_b = 10^{-5}$$

Skewness and kurtosis of fitness fluctuations



$$s_b = 0.05, U_b = 10^{-5}$$

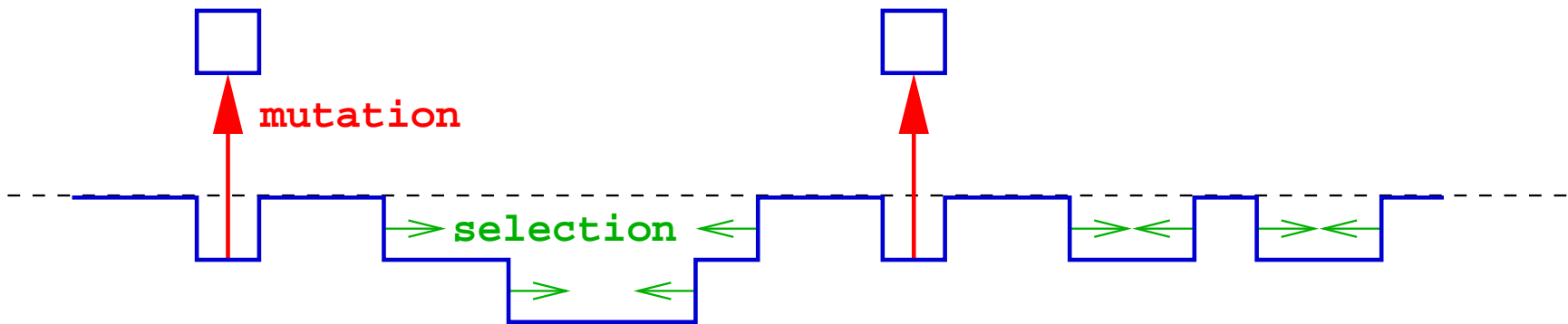
Universal fitness distributions



- Dimensionless RV determined from $\chi = \frac{\ln w - Vt}{(\vartheta t)^{1/3}}$ with numerically fitted parameters V and ϑ
- Blue squares show data for exponential distribution of selection coefficients

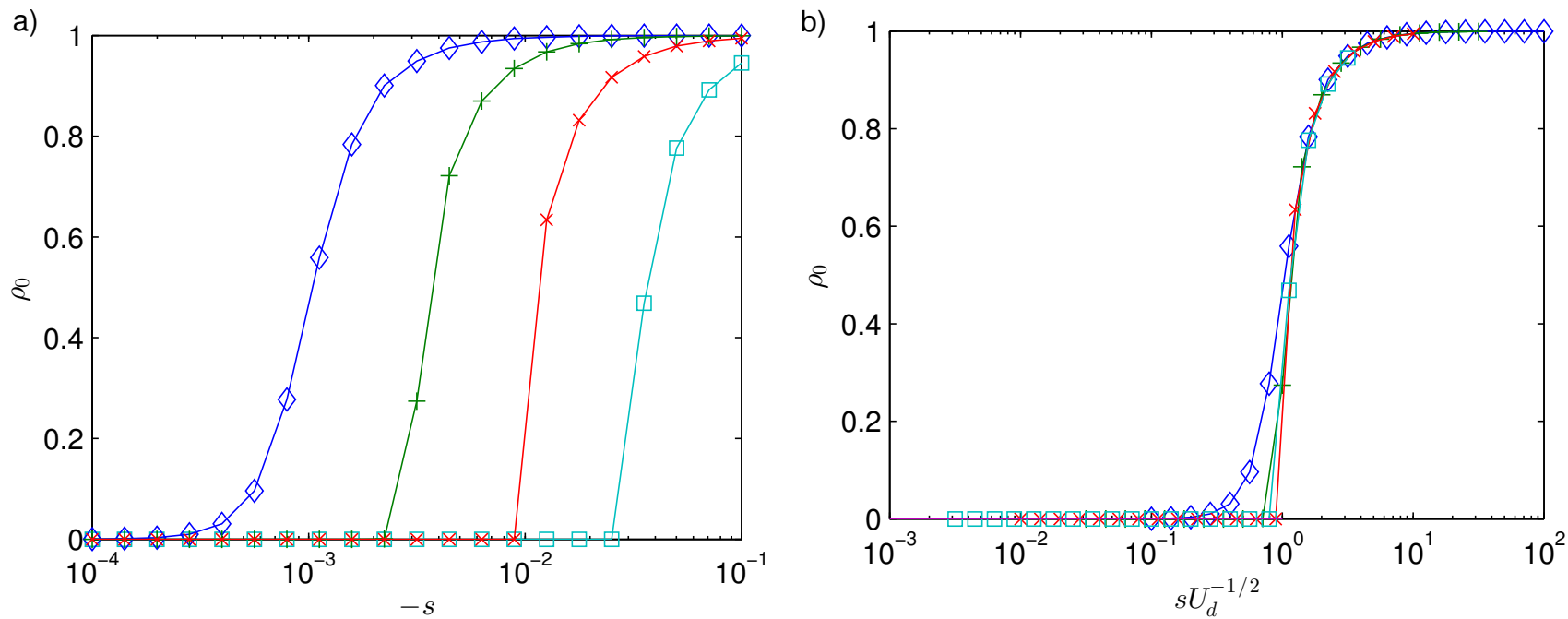
Deleterious mutations

- In the surface analogy deleterious mutations ($s < 0$) punch holes that are closed by selection:



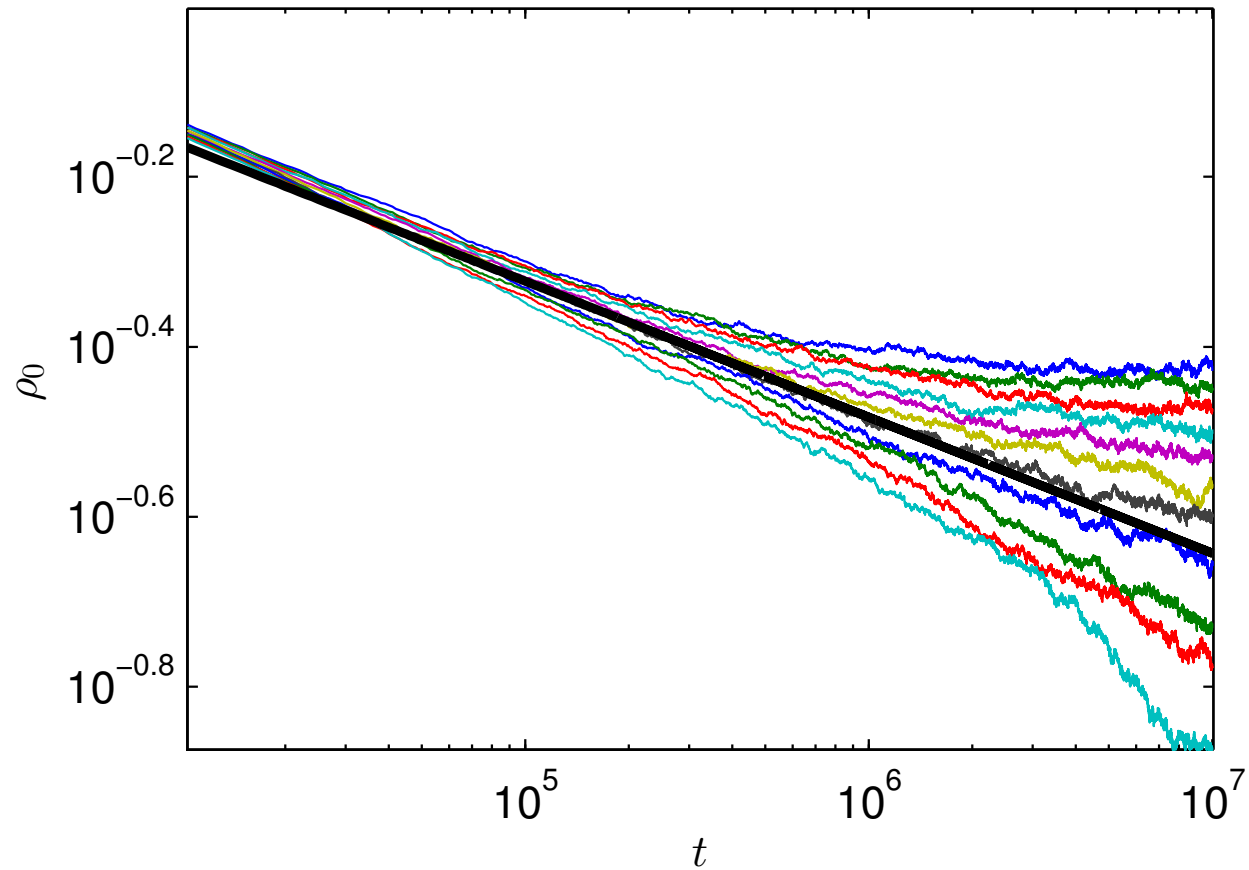
- For small $U = U_d$ holes appear and heal independently
⇒ fraction of sites ρ_0 with zero mutations is reduced by $1 - \rho_0 \sim U_d/s^2$
- Holes percolate and cause a steady fitness decline when $u \equiv U_d/s^2 \approx 1$
- Known as **Muller's ratchet** in population genetics and **nonequilibrium wetting** in growth models
Kertész & Wolf 1989; Alon et al. 1996

Fraction of non-mutated sites in steady state



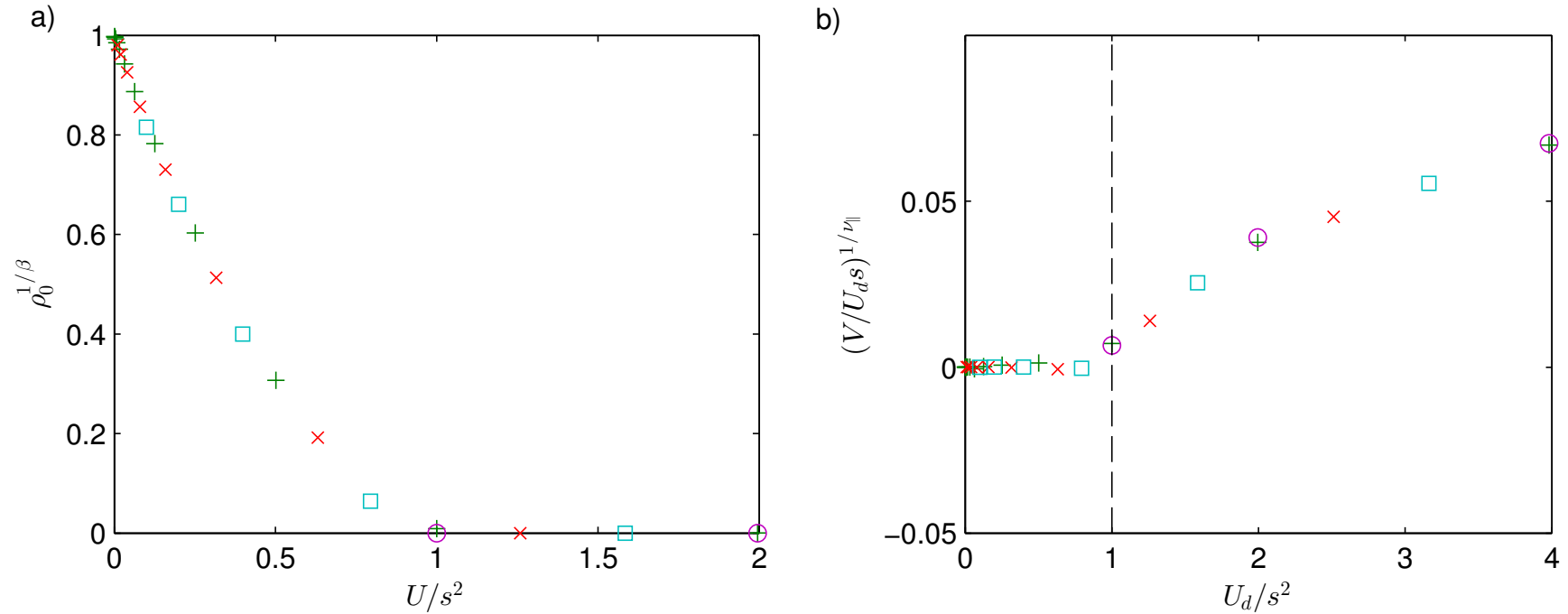
$$U_d = 10^{-6}, 10^{-5}, 10^{-4}, 10^{-3}$$

Fraction of non-mutated sites at the critical point



Prediction of directed percolation (DP) theory: $\rho_0 \sim t^{-\theta}$ with $\theta \approx 0.159464\dots$

Critical behavior consistent with DP exponents



- $\rho_0 \sim (u_c - u)^\beta$ for $u = U_d/s^2 < u_c$, with $\beta \approx 0.276486\dots$
- $V \sim (u - u_c)^{\nu_{\parallel}}$ for $u > u_c$, with $\nu_{\parallel} \approx 1.733847\dots$

Summary

- Two biological realizations of KPZ universality:
 - morphology of genetic clones in growing bacterial colonies
 - fitness dynamics of populations adapting in a spatial habitat
- Surface growth analogies for two important evolutionary scenarios:
 - clonal interference \simeq kinetic roughening
 - Muller's ratchet \simeq nonequilibrium wetting

Lessons for evolutionary biology

- Local competition in spatial systems reduces the strength of selection, leading to
 - a limit on the speed of adaptation
 - a finite rate of fitness decline for infinite populations
 - a reduction of the threshold for Muller's ratchet from $U_d \sim |s|$ to $U_d \sim s^2$