Stochastic neutral fractions

&

the effective population size.

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1) STOCHASTIC NEUTRAL FRACTIONS

The Wright-Fisher model

- fixed population size $N \in \mathbb{N}$
- discrete time t

<u>ex</u> : $N = 4$.

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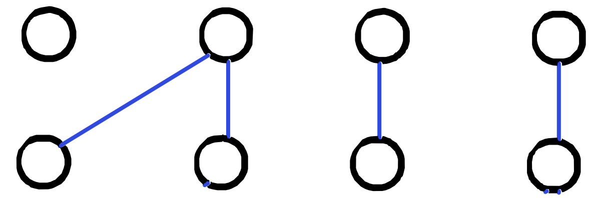

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  the population is renewed
  each individual uniformly at random, independently of the other individuals

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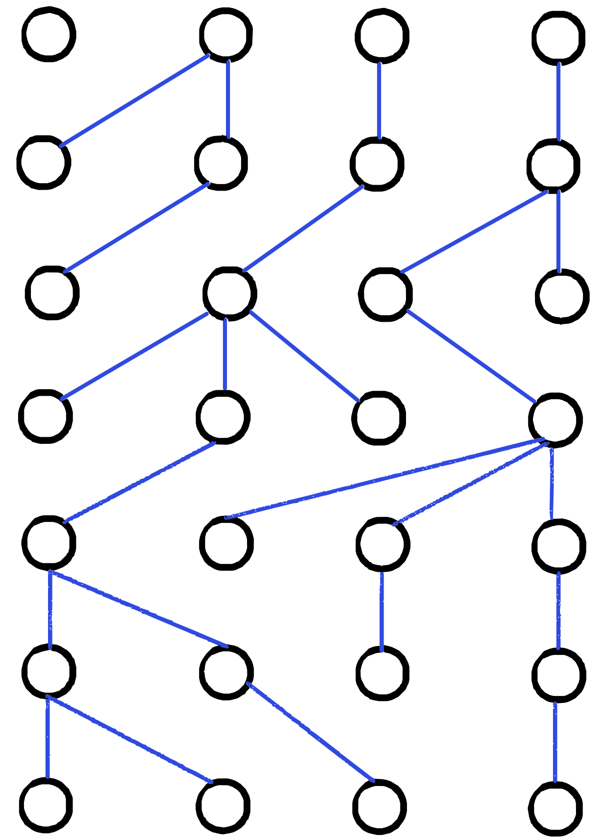


<u>ex</u>: $N = 4$.

1) STOCHASTIC NEUTRAL FRACTIONS

Neutral fractions

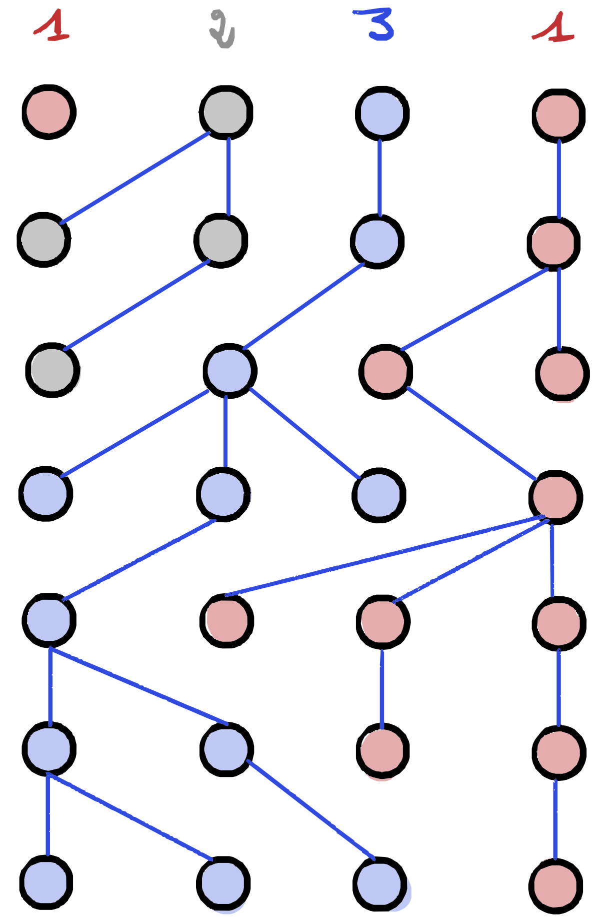
- at $t=0$, each individual is assigned an allele / colour indexed by

$$\underbrace{[K]}_{\sim} = \{1, 2, \dots, K\}$$

$K \in \mathbb{N}$ number of alleles

- $t \in \mathbb{N}$, each individual inherits the allele of its parent

↳ alleles are neutral



$X_t^{N,1} = 1/4$ $\quad X_t^{N,2} = 0$

$X_t^{N,3} = 3/4$

For $i \in [K]$, $t \in \mathbb{N}_0$

$$X_t^{N,i} = \text{frequency of allele } i \text{ at generation } t.$$

Asymptotic behaviour of $(X_t^{i,N}, i \in [K], t \in \mathbb{N})$ as $N \to +\infty$?

1) STOCHASTIC NEUTRAL FRACTIONS

$X_t^{N,i}$: frequency of type i at time t. / size of the i-th fraction

Assume that the initial frequencies converge to a non degenerate limit $(X_0^{N,i} ; i \in [K]) \Rightarrow x_0 \in [0,1]^K$. Then, as $N \to +\infty$,

$$(X_{\lfloor tN \rfloor}^{N,i} ; i \in [K], t \geq 0) \Longrightarrow (Z_t^i ; i \in [K], t \geq 0)$$

$(K-1)$ dimensional standard Wright-Fisher diffusion (*)

(*) diffusion on the simplex $\{(z_1, \dots, z_K) \in [0,+\infty)^K : \sum z_k = 1\}$ with infinitesimal generator

$$\mathcal{L} f(z) = \frac{1}{2} \sum_{1 \leq i,j \leq K} (\delta_{ij} z_i - z_i z_j) \frac{\partial^2}{\partial z_i \partial z_j} f(z)$$

1) STOCHASTIC NEUTRAL FRACTIONS

WF model : Well-mixed population

equal chances of reproductive success

"fluctuations in the allelic composition only due to genetic drift"

(?) Impact of ecological constraints on genetic compositions

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* individuals carry types (spatial locations / fitness)
* each type corresponds to a different ability to reproduce
* non-local reproduction (migrations / mutations)

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Backward-in-time approach

structured coalescents $\xrightarrow[\text{timescales} \quad N \to \infty]{\text{Separation of}}$ Kingman's coalescent on timescale N_e

↓ duality

Wright-Fisher diffusion on timescale N_e

1) STOCHASTIC NEUTRAL FRACTIONS

N_e : effective population size.

"size of the WF diffusion that experiences the same level of genetic drift as the structured population"

Questions ?

* What if there is no separation of timescales ?

  or the population size is not fixed ?

* can we use the backward approach ? Not so easy !

GOAL : Define a general framework to work directly with neutral fractions in structured models.

1) (STOCHASTIC) NEUTRAL FRACTIONS IN THE FKPP EQUATION

The FKPP equation

$$\boxed{\partial_t u = \frac{1}{2}\partial_{xx} u + r(u)u \qquad (PDE_1)}$$

$u(t,x)$ density of individuals at time t at $x \in \mathbb{R}$ = type

$r(u)$: per capita growth rate $\Rightarrow$ density dependent

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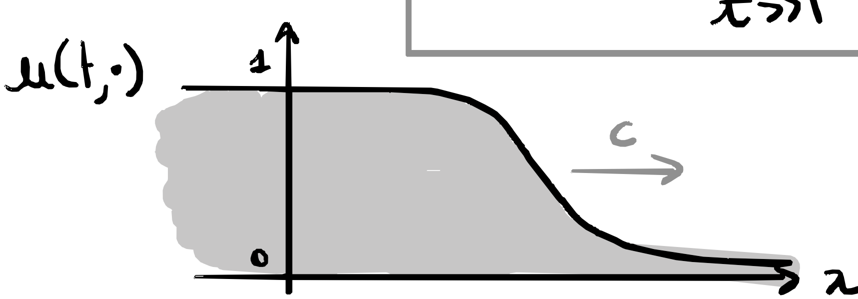
Asymptotic behaviour

There exists a minimal speed c, and an associated profile $\tilde{h}$ s.t

under suitable i.c.,

$$\boxed{u(t,x) \underset{t \gg 1}{\approx} \tilde{h}(x-ct)}$$

travelling wave/front solution to (PDE$_1$)



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How to define neutral fractions ?

Hallatschek and Nelson 2008

Roques, Garnier, Hamel and Klein 2012

initial condition : $u(0,x) = u_0(x) = \sum_{k=1}^{K} v_0^k(x)$

fraction dynamics : for all $k \in [K]$, v^k solution to the PDE

$$\boxed{\begin{cases} \partial_t v^k = \frac{1}{2}\partial_{xx} v^k + r(u)\,v^k \\ v^k(0,x) = v_0^k(x) \end{cases} \qquad (\mathrm{PDE}_2)}$$

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$\sum v^k$ solution to (PDE_1)

AND

same dispersal + same growth $\Rightarrow$ neutral fractions

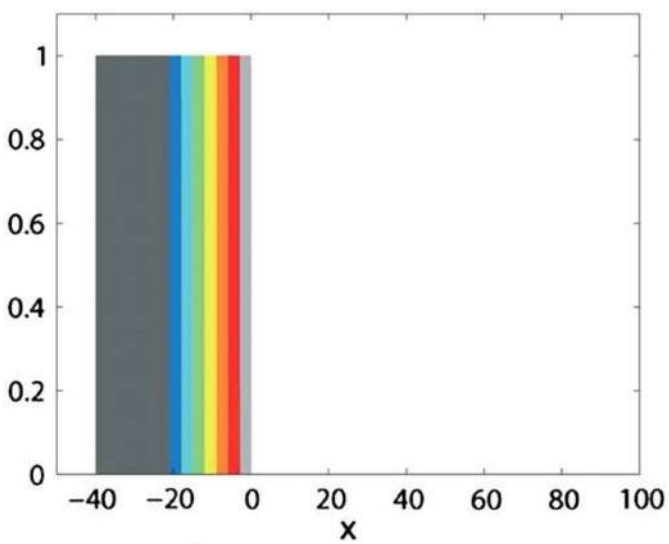
1) (STOCHASTIC) NEUTRAL FRACTIONS IN THE FKPP EQUATION

$$\partial_t u = \frac{1}{2}\partial_{xx} u + r(u)\, u \quad \text{(PDE}_1\text{)}$$ Total population size

$$\partial_t v^k = \frac{1}{2}\partial_{xx} v^k + r(u)\, v^k \quad k \in [K] \quad \text{(PDE}_2\text{)}$$ neutral fractions

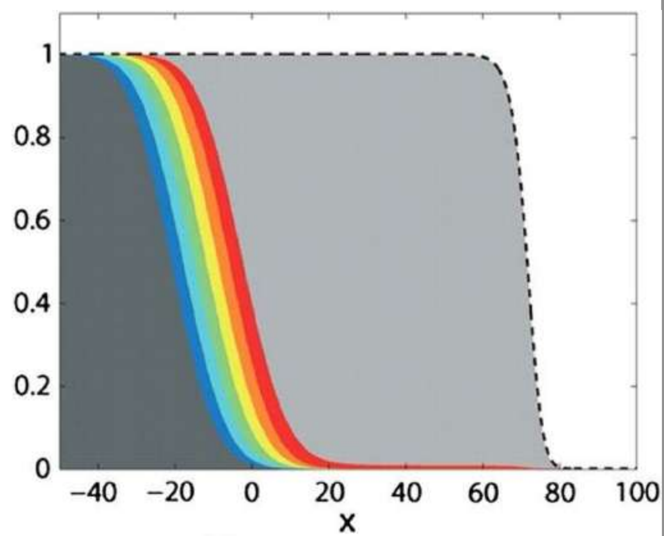
Roques, Garnier, Hamel and Klein 2012

$t = 0$



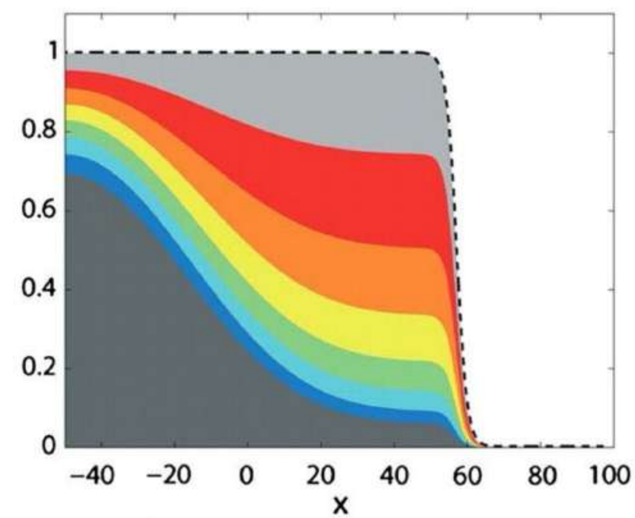
EX 1

$r(u) = (1-u)$



EX 2 : Allee effects

$r(u) = (1-u)(u-u^*)$



1) {STOCHASTIC} NEUTRAL FRACTIONS IN THE FKPP EQUATION

Noisy FKPP equation :

$$\boxed{\partial_t u^N = \frac{1}{2}\partial_{xx} u^N + r(u^N)\,u^N + \sqrt{\frac{u^N}{N}}\,\dot{W}} \quad (SPDE_1)$$

N : large demographic parameter local population density

$\dot{W}$: white noise

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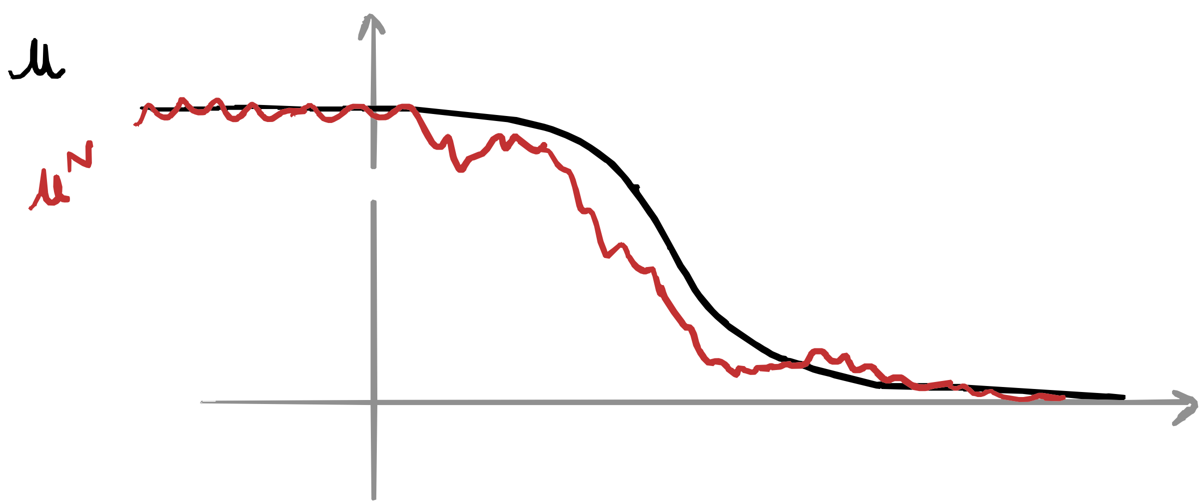
1st step : fluctuations of the total population u^N around the deterministic limit $(N \to +\infty)$?

↳ HARD PROBLEM !



2) THE MODEL

$E = (x_1, \dots, x_d)$ finite type space

We consider the d-dimensional stochastic differential equation

$$\boxed{dU_t^N = b(U_t^N)\,dt + \frac{1}{\sqrt{N}}\, a(U_t^N)\, dW_t} \quad (SDE_1)$$

$U_t \in \mathbb{R}^E$, $\forall x \in E$ $(U_t)_x$ "number" of individuals with type x

$b : \mathbb{R}^E \longrightarrow \mathbb{R}^E$ growth of the system

$a : \mathbb{R}^E \longrightarrow M_d(\mathbb{R})$ noise correlation matrix

W_t d-dimensional Wiener process.

a and b are smooth enough to have existence + uniqueness of weak sol.

How to define neutral fractions in this population model?

2) THE MODEL

Neutral fractions. Can we define $\forall K \in \mathbb{N}$ $V_t^1, \dots, V_t^K : \mathbb{R}^+ \times \mathbb{R}^E \longrightarrow \mathbb{R}^E$ s.t.

1) $\sum_{k=1}^{K} V_t^k$ is solution to (SDE$_1$) "fractions"

2) the fractions are exchangeable : $\forall \sigma \in S_K$

$$\boxed{\left(V_t^{\sigma(1)}, \dots, V_t^{\sigma(K)}\right) \overset{\mathcal{L}}{=} \left(V_t^1, \dots, V_t^K\right)}$$

"neutral"

3) the fractions are consistent

$$\boxed{\left(V_t^1, \dots, V_t^{K-1} + V_t^K\right) \overset{\mathcal{L}}{=} \left(V_t^1, \dots, V_t^{K-1}\right)}$$

1) + 2) + 3) : the system is ∞-decomposable

2) THE MODEL

Sufficient conditions for (SDE$_1$) to be ∞-decomposable

(1) DRIFT TERM

$\exists F : \mathbb{R}^E \to \mathcal{L}(\mathbb{R}^E, \mathbb{R}^E) : \forall U \in \mathbb{R}^E,$ $\boxed{b(U) = F(U)\,U}$

remark : density-dependent growth rate $\approx$ FKPP $r(u)\,u$

(2) DEMOGRAPHIC FLUCTUATIONS

$\exists C : \mathbb{R}^E \to \mathcal{L}(\mathbb{R}^E, \mathcal{L}(\mathbb{R}^E, \mathbb{R}^E))$ and $\sigma : \mathbb{R}^E \times \mathbb{R}^E \to M_{d,K}(\mathbb{R})$.

such that $\forall U_1, U_2 \in \mathbb{R}^E,$

$$\boxed{aa^*(U_1) = C(U_1).U_1 \quad \text{and} \quad \sigma\sigma^*(U_1, U_2) = C(U_1)\,U_2}$$

Neutral fractions $(V_t^1, \dots, V_t^K)$ solutions to

$$\boxed{dV_t^{N,k} = F\left(\sum V_t^{N,k}\right) V_t^{N,k} + \frac{1}{\sqrt{N}}\, \sigma\left(\sum V_t^{N,k}, V_t^{N,k}\right) dW_t^k \;;\; k \in [K] \quad (\text{SDE}_2)}$$

(W_t^k) independent d-dimensional Wiener processes

$$\boxed{dV_t^{N,k} = F\left(\sum V_t^{N,k}\right) V_t^{N,k} + \frac{1}{\sqrt{N}}\, \sigma\left(\sum V_t^{N,k}, V_t^{N,k}\right) dW_t^k \;;\; k \in [K]} \quad (SDE_2)$$

Katzenberger 90':

Assume that the deterministic system

$$\boxed{dV_t^k = F\left(\sum_{k=1}^{K} V_t^k\right) V_t^k \quad k \in [K],\ t>0} \quad (ODE_2)$$

has an attractive stable manifold Γ.

Then, as $N \to +\infty$, on a suitable time scale, $(V_t^{N,k};\ k \in [K])$ converges to a diffusion on Γ

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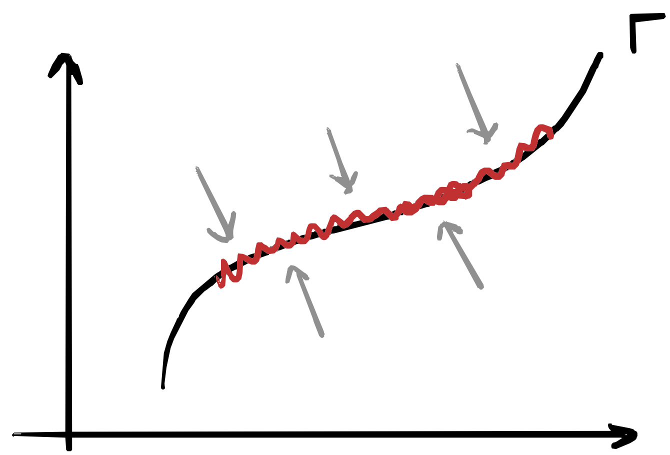
Then, as $N \to +\infty$, on a suitable time scale, $\left(V_t^{N,k} ; k \in [K]\right)$ converges to a diffusion on Γ

⊕ (SDE_2) does not necessarily satisfies the ∞-decomposability condition

⊖ the limiting diffusion is not explicit.



Assumptions

$$du_t^N = b(u_t^N)\,dt + \frac{1}{\sqrt{N}}\,a(u_t^N)\,dW_t \qquad \text{(SDE}_1\text{)}$$

(∞-decomposability) $\quad b(u) = F(u)u$ and $aa^*(u) = C(u)u$.

(regularity) $\quad F$ and C are smooth

(equilibrium) $\quad \frac{du_t}{dt} = b(u_t)$ (ODE$_1$) has an exponentially locally attractive equilibrium $\tilde{h} > 0$ $\quad [b(\tilde{h}) = F(\tilde{h})\tilde{h} = 0]$

(PF) $\quad F(\tilde{h})$ is Metzler and $\exists t_0 > 0 : \forall x, y \in E \ (e^{t_0 F(\tilde{h})})_{xy} > 0$

↳ $\tilde{h}$ is the right principal eigenvector associated to $F(\tilde{h})$

↳ there exists an associated positive left eigenvector s.t.

$$\langle h . \tilde{h} \rangle = 1$$

<u>Remark</u>: $\langle \tilde{h} . 1 \rangle \neq 1$ carrying capacity of the system.

3) RESULT

$$\boxed{dV_t^{N,k} = F\left(\sum V_t^{N,k}\right) V_t^{N,k} + \frac{1}{\sqrt{N}}\, \sigma\left(\sum V_t^{N,k}, V_t^{N,k}\right) dW_t^k \;, \quad k \in [K]} \quad (SDE_2)$$

Stable manifold : $\Gamma^K = \left\{ \theta \otimes \tilde{h} \,,\ \sum_{k=1}^{K} \theta^k = 1 \,,\ \theta^k \geq 0 \right\}$

Scaling parameter $\quad \Sigma^2 = \langle h, aa^*(\tilde{h})\, h \rangle$

> **THEOREM** : Under natural assumptions on the initial condition,
>
> $$\left(V^{N,k}_{tN/\Sigma^2} \;;\ k \in [K],\ t \in [0,T] \right) \underset{N\infty}{\Longrightarrow} \left(\theta_t \otimes \tilde{h},\ t \in [0,T] \right)$$
>
> where (θ_t) is a standard $(K-1)$-dimensional Wright–Fisher diffusion

$N_e = \dfrac{N}{\Sigma^2}$ $\qquad$ effective population size.

3) RESULT

$$\boxed{du_t^N = b(u_t^N)\,dt + \frac{1}{\sqrt{N}}\,a(u_t^N)\,dW_t} \quad (SDE_1)$$

$$\boxed{dv_t^{N,k} = F\left(\sum v_t^{N,k}\right) v_t^{N,k} + \frac{1}{\sqrt{N}}\,\sigma\left(\sum v_t^{N,k}, v_t^{N,k}\right) dW_t^k \;;\; k \in [K]} \quad (SDE_2)$$

<u>EX</u> $\approx$ Noisy FKPP equation

$$a(u) = \begin{pmatrix} \sqrt{u_1} & & 0 \\ & \ddots & \\ 0 & & \sqrt{u_d} \end{pmatrix}$$

then

$$C(u)\,u = \begin{pmatrix} u_1 & & 0 \\ & \ddots & \\ 0 & & u_d \end{pmatrix} \quad \text{and} \quad \sigma(u,w) = \begin{pmatrix} \sqrt{w_1} & & 0 \\ & \ddots & \\ 0 & & \sqrt{w_d} \end{pmatrix}$$

$$\Sigma^2 = \sum_{x \in E} h_x^2\,\tilde{h}_x \qquad (N_e = N/\Sigma^2)$$

reproductive variance of the structured system.

$\tilde{h}_x$: mean number of children of an individual with type x.

5) What do we expect for stochastic FKPP equations ?

$$\boxed{\partial_t u^N = \frac{1}{2}\partial_{xx} u^N + r(u^N)u^N + \sqrt{\frac{u^N}{N}}\,\dot{W}(t)} \quad \text{(SPDE}_1\text{)}$$

(equilibrium) there exists a stable profile $\tilde{h}$ such that

$$\| u^\infty(t, \cdot + ct) - \tilde{h}(\cdot) \|_\infty \leq C e^{-\lambda t}$$ [√ Allee case]

(finite variance) $$\Sigma^2 = \int_{\mathbb{R}} h(x)^2 \tilde{h}(x)\, dx < +\infty$$ [√ Allee case]

Then $\exists (\xi_t^N)_{t\geq 0}$ s.t

$$\boxed{\begin{array}{l} \sup_{t\in[0,TN]} \| u^N(t,\cdot) - \tilde{h}(\cdot - \xi_t^N) \| \xrightarrow[N\infty]{} 0 \\ (\xi_t^N) \text{ converges to a Brownian motion} \end{array}}$$

Etheridge, Forien, Penington 2025+

and

$$\boxed{\sup_{t\in[0,TN]} \sup_{k\in[K]} \| v^{k,N}(t,\cdot) - \underbrace{\theta^{k,N}(t)}_{\text{WF ?}} \tilde{h}(\cdot - \xi_t^N) \| \xrightarrow[N\infty]{} 0}$$

4) SKETCH OF PROOF

notation $\quad V_t^N = (V_t^{N,1} \dots V_t^{N,K})$ composition matrix $\in M_{d,K}(\mathbb{R}^+)$

Katzenberger projection π

let $\Phi : [0,+\infty) \times M_{d,K}(\mathbb{R}^+) \longrightarrow M_{d,K}(\mathbb{R}^+)$

$$(t, v_0) \longmapsto \Phi(t, v_0) = v_t$$

where v_t is solution of the ODE

"flow of the deterministic dynamics"

$$\boxed{\begin{array}{l} \dot{v}_t = F\left(\sum_{j=1}^{K} v_t^j\right) v_t \\ \text{initial condition } v_0 . \ (ODE_2) \end{array}}$$

Define $\pi(v_0) = \lim_{t \to +\infty} \Phi(t, v_0)$

Fact 1 : $\pi(v_0) \in \Gamma^K \Rightarrow \pi(V_t^N)$ natural candidate for the limiting diffusion.

$\lightning$ It usually requires a lot of info on the flow to work with π.

4) SKETCH OF PROOF

notation $V_t^N = (V_t^{N,1} \dots V_t^{N,k})$ composition matrix $\in M_{d,k}(\mathbb{R}^+)$

Katzenberger projection $\pi(\cdot) = \lim_{t \to +\infty} \Phi(t, \cdot)$

Fact 1 : $\pi(v_0) \in \Gamma^K$ $\Rightarrow$ $\pi(V_t^N)$ natural candidate for the limiting diffusion.

Fact 2 $\exists H : \mathbb{R}^d \longrightarrow \mathbb{R}^d$ such that

$\forall v_0 \in M_{d,k}(\mathbb{R}^+)$ $\boxed{\pi(v_0)^j = \langle H(u_0), v_0^j \rangle \tilde{h}}$ $u_0 = \sum v_0^j$

Proof. decomposability $\Rightarrow$ each column is solution of a linear ODE

$\rightsquigarrow$ Reduction of the problem's dimension

Next steps of the proof : 1) show that $V_t^N \approx \pi(V_t^N)$ STABILITY.

2) show that $(\langle H(U_t^N), V_t^{N,j} \rangle)_j \Rightarrow WF$

ITÔ CALCULUS.

4) SKETCH OF PROOF

Stability: show that $\pi(V_t^N) \approx V_t^N$

$\mathbb{R}^d \ni w$ right e.v

Define the Perron-Frobenius projection $P : w \longmapsto \langle w, h \rangle \tilde{h}$

left e.v.

0) Stability of the total pop. size $U_t^N \approx \tilde{h}$

1) Stability of Perron-Frobenius dynamic projections

$$\left(P(V_t^{N,i})\right)_i \approx V_t^N$$

Proof. Standard Perron-Frobenius theory + martingale arguments.

2) Comparison with Katzemberger projections

Recall that $\pi(V_t^N)^i = \langle H(U_t^N), V_t^{N,i} \rangle \tilde{h}$.

$$\| H(v_0) - h \| \leq C \| v_0 - \tilde{h} \|$$