Haldane's formula in Cannings models with moderate selection

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Haldane's formula

Haldane's formula is a rough-and-ready rule
for the fixation probability π of a slightly advantageous allele
initially present in a single individual in a large population:

$$\pi \approx \frac{s}{v/2}$$

with s the selective advantage,
and v the individual offspring variance per generation.

Spreading like a branching process

In a large population an advantageous allele spreads initially like a supercritical branching process. The survival probability of a (slightly) supercritical branching process obeys Haldane's formula:

Theorem (Athreya 1992)

Let $(Z^{(N)})_{N\geq 1}$ be a sequence of supercritical Galton-Watson processes with offspring mean $1 + s_N \to 1$, offspring variance $v_N \to v$ and uniformly bounded third moment, starting with a single individual in generation 0.
Then the survival probability π_N of $Z^{(N)}$ fulfills

$$\pi_N \sim \frac{s_N}{v/2}.$$

Diffusion setting

$s_N = \frac{\alpha}{N}$, x initial frequency of advantageous allele

Kimura's formula

$$\pi = \frac{1 - e^{-2\alpha x}}{1 - e^{-2\alpha}}.$$

Set $x = \frac{1}{N}$

$$\frac{1 - e^{-2\alpha x}}{1 - e^{-2\alpha}} = \frac{1 - e^{-2s_N}}{1 - e^{-2\alpha}} \sim \frac{2s_N}{1 - e^{-2\alpha}}$$

Today

- **Moderate selection $s_N \sim N^{-b}$ for $0 < b < 1$**
  Covers a broad range of selection strengths
- **Discrete time models**
  Model populations with seasonal behaviour, experimental evolution, ...
  Cannings models with selection

Neutral Cannings model

- constant population size N
- discrete generations $g = 1, 2, \ldots$
- exchangeable offspring numbers
  - each child chooses a parent in the previous generation
  - $\xi_i^{(g)}$ - the number of children of the i-th parent in generation g, $i = 1, \ldots, N$
  - $\sum_{i=1}^{N} \xi_i^{(g)} = N$
  - $\xi_1^{(g)}, \ldots, \xi_N^{(g)}$ exchangeable.
- time homogeneous: $(\xi^{(g)})_{g=1,2,\ldots}$ are iid

Most prominent Cannings model: Wright-Fisher model

Parents are chosen independently and uniformly among all individuals in the previous generation

$$(\xi_1^{(g)}, \ldots, \xi_N^{(g)}) \stackrel{d}{=} \text{Multinom}(N; 1/N, \ldots, 1/N).$$

A subclass of neutral Cannings models

For each g let $\mathcal{W}^{(g)} = (W_1^{(g)}, \ldots, W_N^{(g)})$ be a random exchangeable *mass partition of* 1, that is

$$W_i^{(g)} \geq 0 \qquad \text{and} \qquad \sum_{i=1}^{N} W_i^{(g)} = 1.$$

Assume $(\mathcal{W}^{(g)})_{g=0,1,\ldots}$ are iid.

$$(\xi_1^{(g)}, \ldots, \xi_N^{(g)}) \stackrel{d}{=} \text{Multinom}(N; W_1^{(g)}, \ldots, W_N^{(g)}).$$

These models mimic e.g. the following reproduction cycle

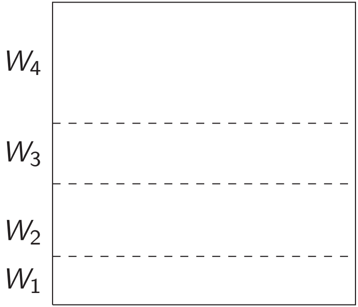
- Assume parents $i = 1, ..., N$ have large iid random numbers $Y_1, ..., Y_N$ of offspring in generation g.
- Only N of these offspring survive till generation $g + 1$.
- The individuals (the children) which survive are drawn randomly from all offspring.
- If the number of offspring is large, drawing with and without replacement is approximately the same.
- Hence, the probability that the i-th child is an offspring parent j is approximately

$$W_j = \frac{Y_j}{Y_1 + ... + Y_N}$$

for $i = 1, ..., N$.

A graphical description of the Cannings model

$\mathbb{P}($ Child i chooses j as parent $|\mathcal{W}) = W_j$, for $i = 1, ..., N$ independently.



with $U_i \sim$Unif$[0,1]^2$, $i = 1, ..., N$, and independent.

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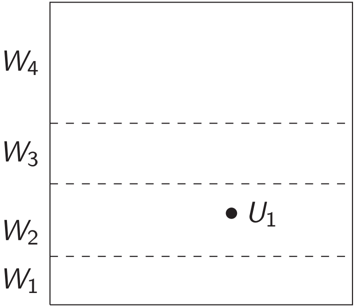

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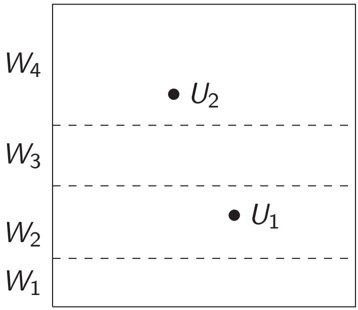

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A Wright-Fisher model with selection

- Constant population size N with 2 types: wild type and beneficial type
- s_N selection strength, $0 < s_N < 1$.
- give beneficial individuals weight 1
- give wild type individuals weight $1 - s_N$

Cannings models with selection

- Constant population size N with 2 types wildtype and beneficial type.
- s_N selection strength, $0 < s_N < 1$.
- Let $\{W^{(g)}\}_{g \geq 0} = (W_1^{(g)}, ..., W_N^{(g)})_{g \geq 0}$ be an iid exchangeable mass partition of 1.
- Distinguish a neutral part of mass

$$(1 - s_N)W_i$$

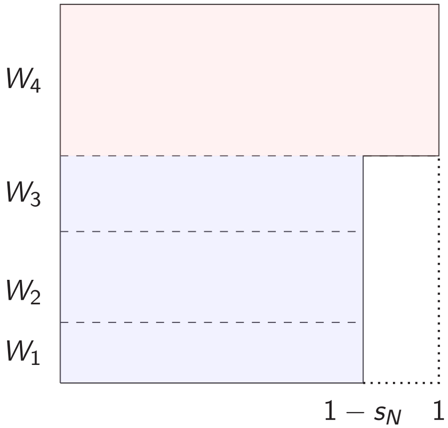
and a selective part of mass

$$s_N W_i$$

for each weight W_i.

Cannings models with selection: forward construction

Assume there are $k \leq N$ wild type individuals.
$U_1, U_2, ..., U_N$ are uniformly distributed on the coloured part.



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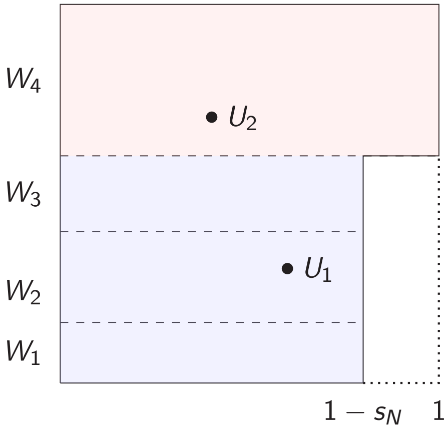
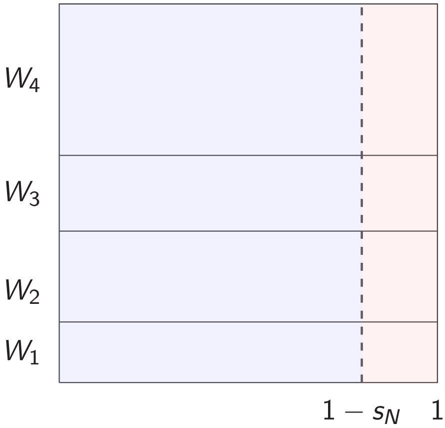


Cannings models with selection: backward construction

- Determine the (exchangeable) weights $W^{(g)} = (W_1^{(g)}, ..., W_N^{(g)})$.
- Don't know types of parents.
- For each individual $1 \leq i \leq N$ throw iid uniforms $(U_i^{(1)}, U_i^{(2)}, ...)$ into $[0,1]^2$ until one falls into the neutral part.
- This leads to a $\text{Geom}(1 - s_N)$ distributed number of potential parents for each individual.



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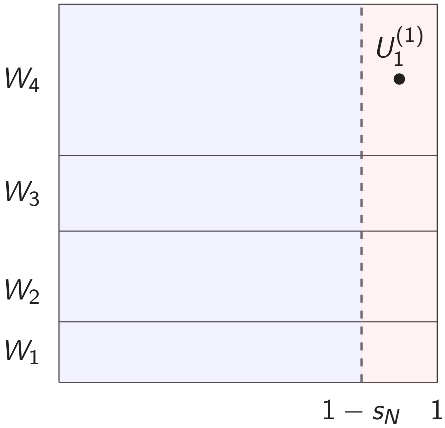

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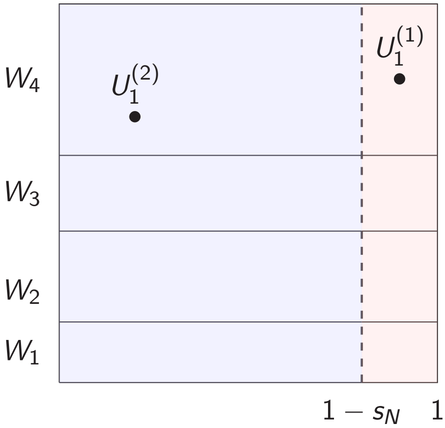

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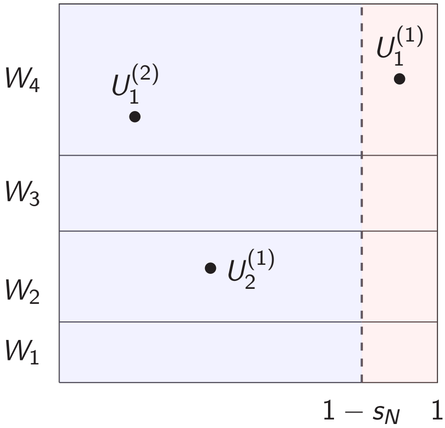

Cannings Ancestral Selection Process

- Proceed further by determining potential ancestors of the potential parents the till generation 0.
- The process $(A_g)_{g\geq 0}$ counts the number of potential parents g generations in the past.
- Colour the individuals in generation 0.
- Propagate types further.

A child has the beneficial type if and only, if
at least one of its potential parents has the beneficial type.

Haldane's formula

- (moderate selection) $s_N \sim N^{-b}$ for $b \in (0,1)$.
  - moderately weak selection $\frac{1}{2} < b < 1$.
  - moderately strong selection $0 < b < \frac{1}{2}$.

Conditions **C**

$$\mathbb{E}\left[W_1^2\right] = \frac{\rho^2}{N^2},\ \rho \geq 1$$

$$\Rightarrow \text{Offspring variance } v_N = \rho^2(1+o(1))$$

$$\mathbb{E}\left[W_1^3\right] = O(N^{-3})$$

- These conditions imply Möhle's criteria for convergence of the genealogies to Kingman's coalescent.

Haldane's formula for $\frac{1}{2} < b < 1$

Let X_g the frequency of wildtype individuals in generation g.
Assume $X_0 = 1 - \frac{1}{N}$.

Theorem

Let $\frac{1}{2} < b < 1$ and the Conditions **C** be fulfilled.
Set

$$T_{fix} = \inf\left\{g \geq 0 : X_g \in \{0,1\}\right\}.$$

Then

$$\pi_N := \mathbb{P}(X_{T_{fix}} = 0) = \frac{2s_N}{\rho^2} + o(s_N).$$

Idea of proof, $b > 1/2$

Sampling Duality

Theorem

Denote by K_g the number of wildtype individuals at time $g \geq 0$ and by A_g the number of potential ancestors g generations back in time. Then

$$\mathbb{E}\left[\frac{K_g(K_g-1)\cdots(K_g-n+1)}{N(N-1)\cdots(N-n+1)}\Big|K_0=k\right]$$
$$=\mathbb{E}\left[\frac{k(k-1)\cdots(k-A_g+1)}{N(N-1)\cdots(N-A_g+1)}\Big|A_0=n\right].$$

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Apply the sampling duality to $k=N-1, n=N$ yields

$$\mathbb{P}(K_g=N|K_0=N-1)=1-\mathbb{E}\left[\frac{A_g}{N}\right]$$

Apply sampling duality

Taking the limit $g \to \infty$ yields

$$\pi_N = \lim_{g \to \infty} 1 - \mathbb{P}(K_g = N | K_0 = N - 1) = \mathbb{E}\left[\frac{A_{eq}}{N}\right].$$

Apply sampling duality

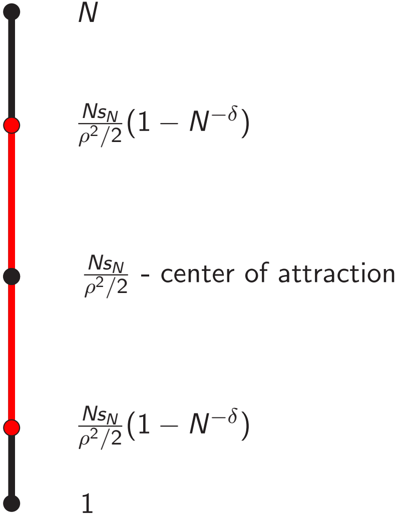
Taking the limit $g \to \infty$ yields

$$\pi_N = \lim_{g\to\infty} 1 - \mathbb{P}(K_g = N | K_0 = N - 1) = \mathbb{E}\left[\frac{A_{eq}}{N}\right].$$

It sufficies to show

$$\mathbb{E}\left[A_{eq}\right] \sim \frac{Ns_N}{\rho^2/2}$$

Concentration of $\mathcal{A} = (A_g)_{g \geq 0}$



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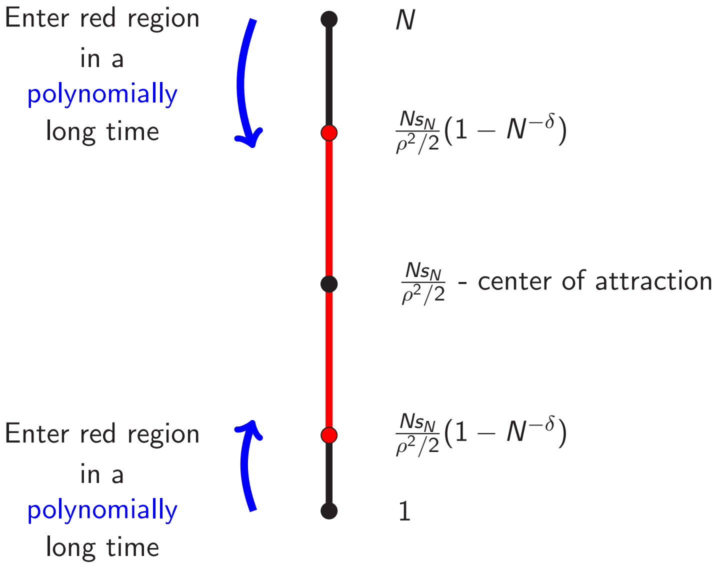

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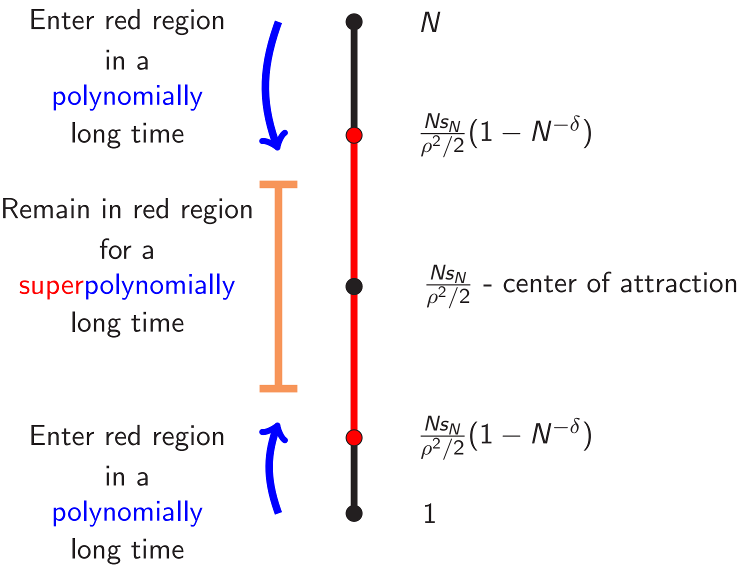

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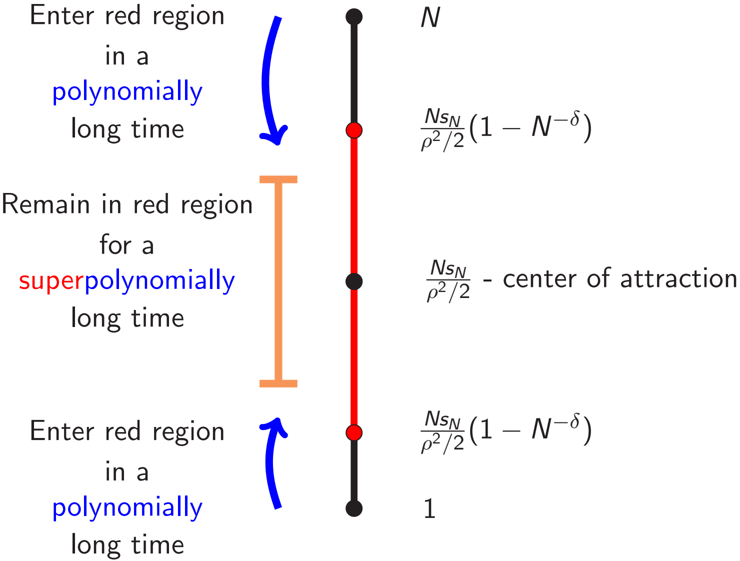

$$\Rightarrow \mathbb{E}[A_{eq}] \sim \frac{Ns_N}{\rho^2/2}$$

Moderately strong selection, $0 < b < \frac{1}{2}$

Dirichlet-type weights

Assume the random weights $\{W_i, 1 \leq i \leq N\}$ are of the form

$$W_i = \frac{Y_i}{\sum_{j=1}^{N} Y_j},$$

with $Y_1, Y_2, \ldots$ iid on $\mathbb{R}^+$

and the following Conditions $\mathbf{C}'$ are fulfilled

- $\mathbb{E}[W_1^2] = \frac{\rho^2}{N^2} + O(N^{-3})$
- For some $h > 0$

$$\mathbb{E}[exp(hY_1)] < \infty.$$

Haldane's formula for $0 < b < \frac{1}{2}$

Let X_g be the frequency of wildtype individuals at time g with $X_0 = 1 - \frac{1}{N}$.

Theorem:

Assume the Conditions **C**' are fulfilled.
Set

$$T_{fix} = \inf\left\{g \geq 0 : X_g \in \{0, 1\}\right\}.$$

Then

$$\pi_N := \mathbb{P}(X_{T_{fix}} = 0) = \frac{2s_N}{\rho^2} + o(s_N).$$

Strategy of proof

(1) Couple the forward process $(X_g)_{g \geq 0}$ to appropriate Galton-Watson processes form above and below to show that the number of beneficial individuals exceeds eventually the level $N^{b+\delta}$ with probability $\frac{2s_N}{\rho^2} + o(s_N)$.

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(2) Show that from $N^{b+\delta}$ the level ϵN is reached with probability $1 - o(s_N)$: Whenever $(X_g)_{g \geq 0}$ is between $N^{b+\delta}$ and $2\epsilon N$, the one-step variance of $(X_g)_{g \geq 0}$ is small enough, such that the exponential increase is strong enough to reach the level ϵN before 0 with probability $1 - o(s_N)$.

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(3) The (equilibrium) backward ancestral process meets with ϵN lines in at least one individual with probability $1 - o(s_N)$ (birthday problem).

Dominating by a Galton-Watson process from above

Assume k individuals are beneficial in generation g. Then since the weights are of Dirichlet-type, in generation $g+1$ the number of beneficial individuals is

$$\mathrm{Bin}\left(N, \frac{\sum_{i=1}^{k} Y_i}{\sum_{j=1}^{k} Y_j + \sum_{j=k+1}^{N}(1-s_N)Y_j}\right) \qquad (1)$$

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For a coupling with Galton-Watson-process need to approximate (1) by a sum of k iid summands.

- **Binom**$(N,p) \leq$ **Pois**(Np):
  $X_1 \sim Ber(p)$, $Y_1 \sim Pois(p)$
  $P(X_1 = 0) = 1 - p \leq e^{-p} = P(Y_1 = 0)$
  Hence, can couple $X \sim Binom(N,p)$ and $Y \sim Pois(Np)$, such that

$$P(X \leq Y) = 1.$$

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  $Pois(\lambda_1 + ... + \lambda_k) = \sum_{i=1}^{k} Pois(\lambda_i)$

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Choose the $p_1, ..., p_k$ for the coupling
As long as $k \leq N^{\frac{1}{2}+\delta}$ we can estimate for sufficiently many generations

$$\frac{\sum_{i=1}^{k} Y_i}{\sum_{j=1}^{k} Y_j + \sum_{j=k+1}^{N}(1-s_N)Y_j} \leq \sum_{i=1}^{k} Y_i \frac{(1+s_N)(1+N^{-\frac{1}{2}+\delta})}{N\mathbb{E}[Y_1]}$$

with probability $1-o(s_N)$.

Gives a coupling from above with a Galton-Watson-process with

$$\frac{(1+s_N)(1+N^{-\frac{1}{2}+\delta})}{N\mathbb{E}[Y_1]} Pois(Y)$$

offspring numbers where $Y \sim Y_1$
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Let $\xi_i^{(g)}$ be the number of offsprings of the i-th beneficial individual in generation g.

$$\xi_1^{(g)} \sim \mathrm{Bin}\left(N, \frac{Y_1(1 + s_N + o(s_N))}{\sum_{i=1}^N Y_i}\right)$$

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Let Z_g be the number of beneficial individuals in generation g. As long as $Z_g \leq N^{\frac{1}{2}}$ this can be lower bounded by

$$\mathrm{Bin}\left(N-N^{\frac{1}{2}}, \frac{Y_j(1+s_N+o(s_N))}{\sum_{i=1}^N Y_i}\right)$$

for each beneficial individual j.

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As long as $Z_g \leq N^{\frac{1}{2}}$ this can be lower bounded with sufficiently high probability by

$$\text{Bin}\left(N - N^{\frac{1}{2}}, \frac{Y_j(1 + s_N + o(s_N))}{N\mathbb{E}[Y_1] + O(N^{\frac{1}{2}-\delta})}\right)$$

for each beneficial individual j.

Idea of proof, $0 < b < \frac{1}{2}$, lower bound

Galton-Watson-process with offspring distribution

$$\text{Bin}\left(N - N^{\frac{1}{2}}, \frac{Y_j(1 + s_N + o(s_N))}{N\mathbb{E}\left[Y_1\right] + O(N^{\frac{1}{2}+\delta})}\right)$$

reaches the level $N^{b+\delta}$ with probability $\frac{2s_N}{\rho^2}(1 + o(1))$.

Summary

For nice Cannings models with selection of strength $s_N \sim N^{-b}$ in the Kingman attraction we proved

- Haldane's formula for $0 < b < \frac{1}{2}$
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