On the spread of an infection in a host population distributed on $\mathbb{Z}$ with host resistance

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joint work in progress
with Sascha Franck

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Spread of an infection with host resistance

- Consider a host population distributed on $\mathbb{Z}$.
- Each site is initially occupied by a single host
- The infection process starts in the origin $0 \in \mathbb{Z}$.
  A pathogen infects the host at the origin
- The first infection is successful, in the sense that the host dies and offspring pathogens are generated
- Pathogens perform independent symmetric random walks with step size ± 1.
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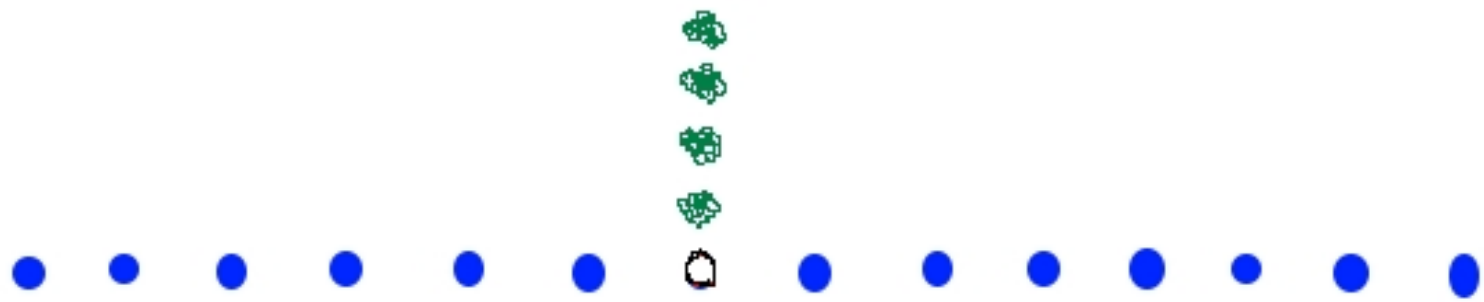

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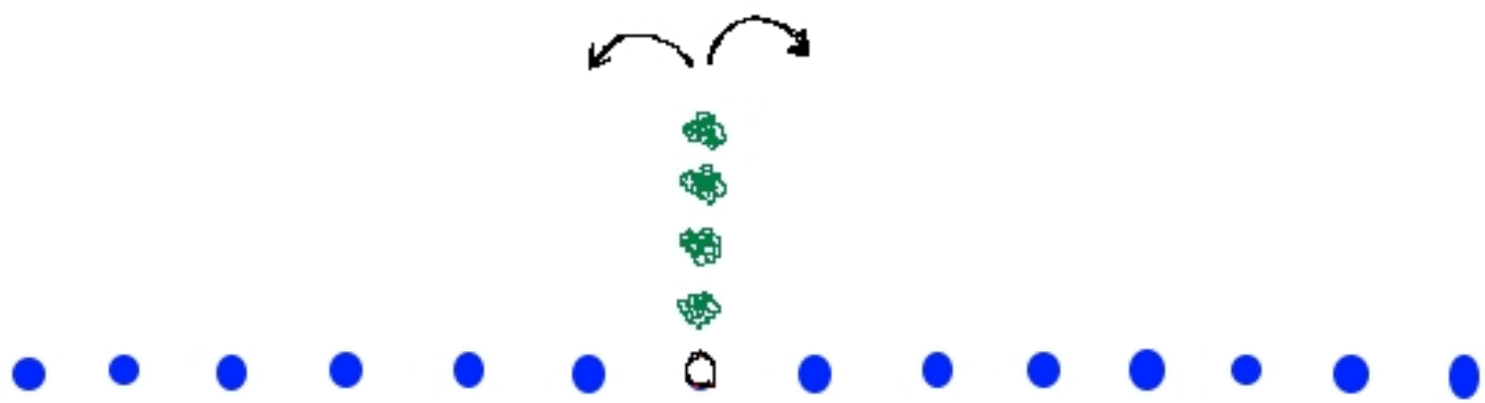

Spread of an infection with host resistance

- A host can resist against the infection at some strength $\in \mathbb{N}$.
  If the resistance of a host is larger than 1, the host stays alive, the pathogen dies and the resistance reduces by one.
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- Sites free of hosts can be occupied by several pathogens.
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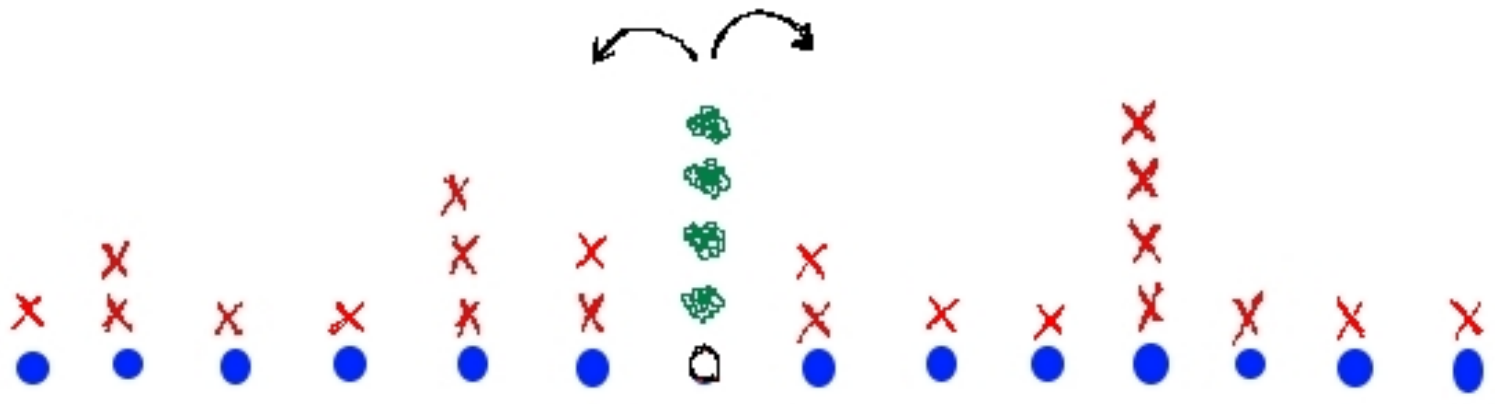

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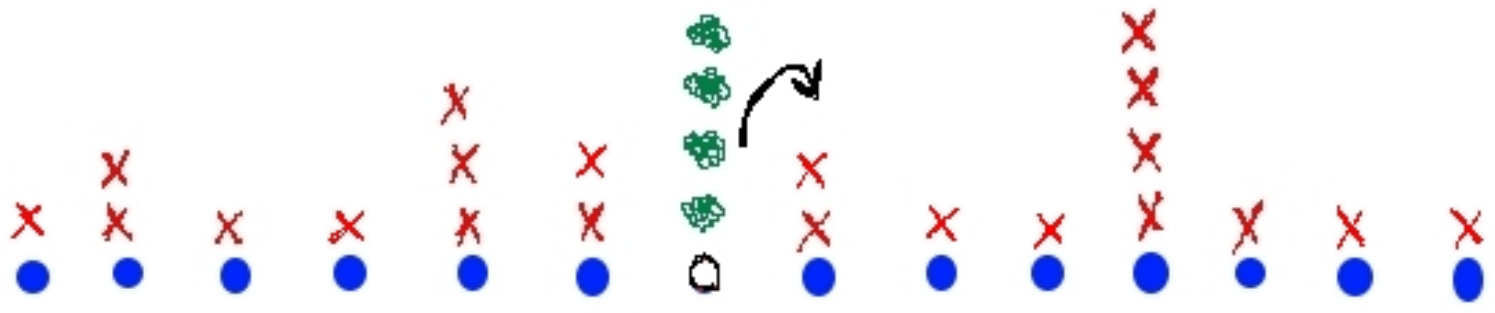

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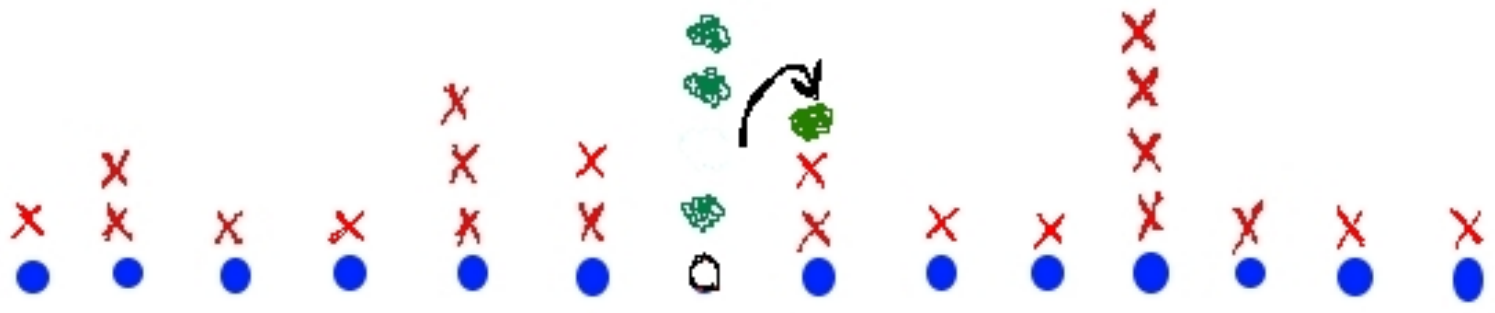

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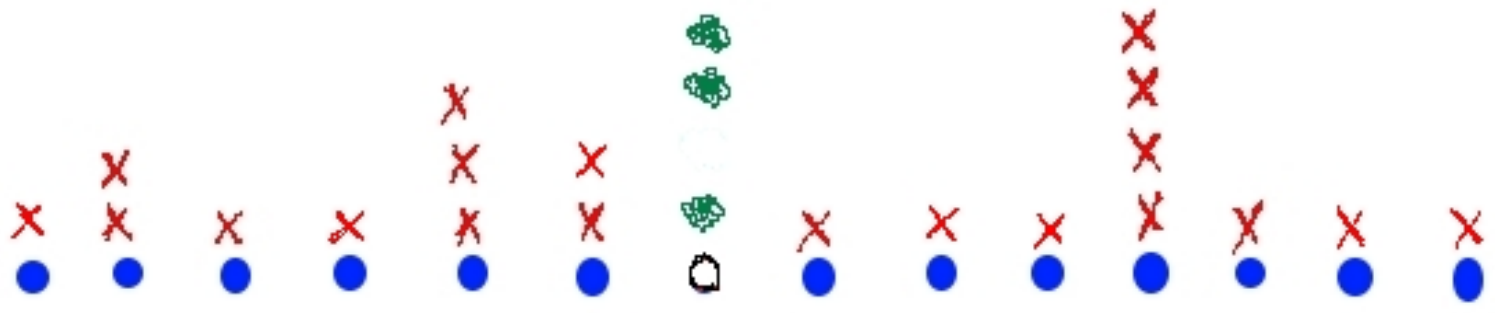

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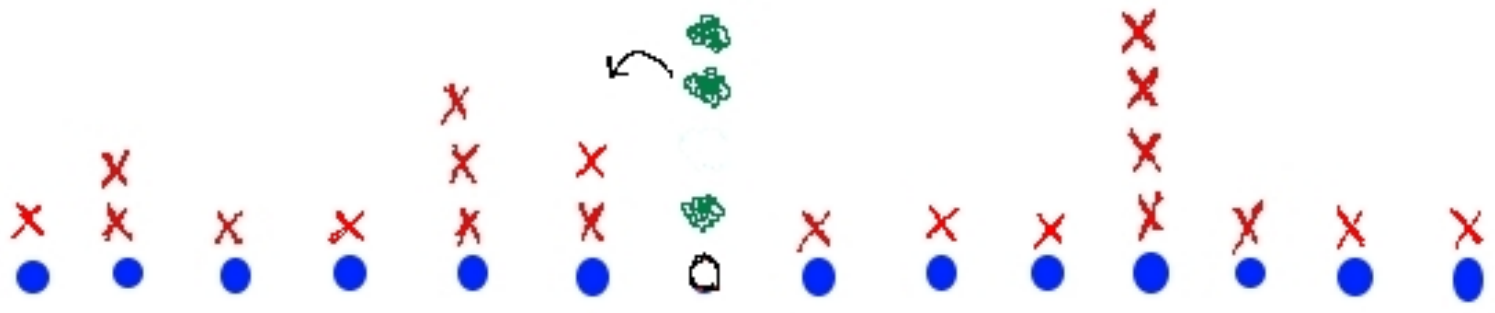

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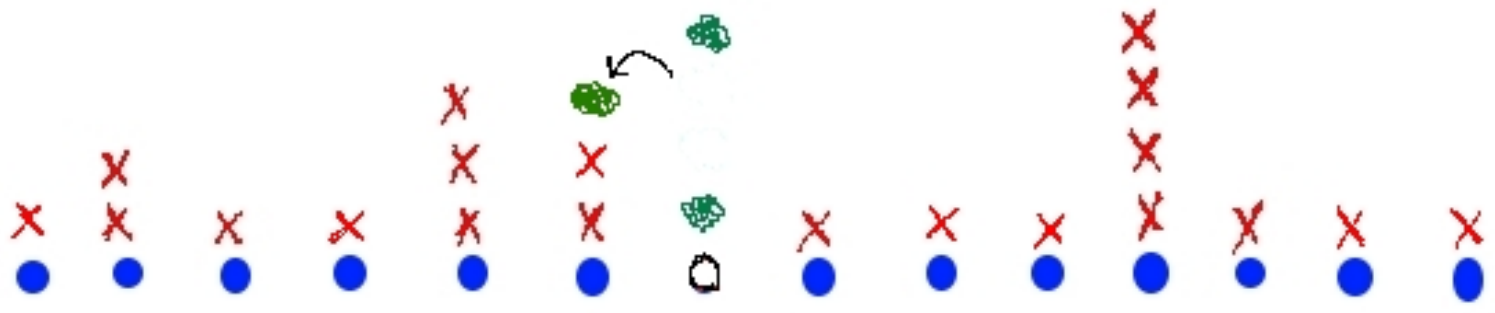

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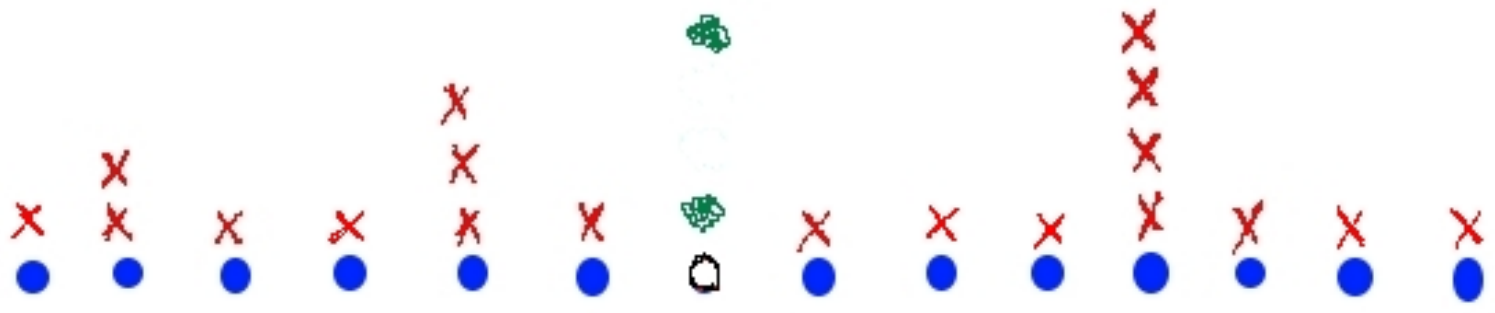

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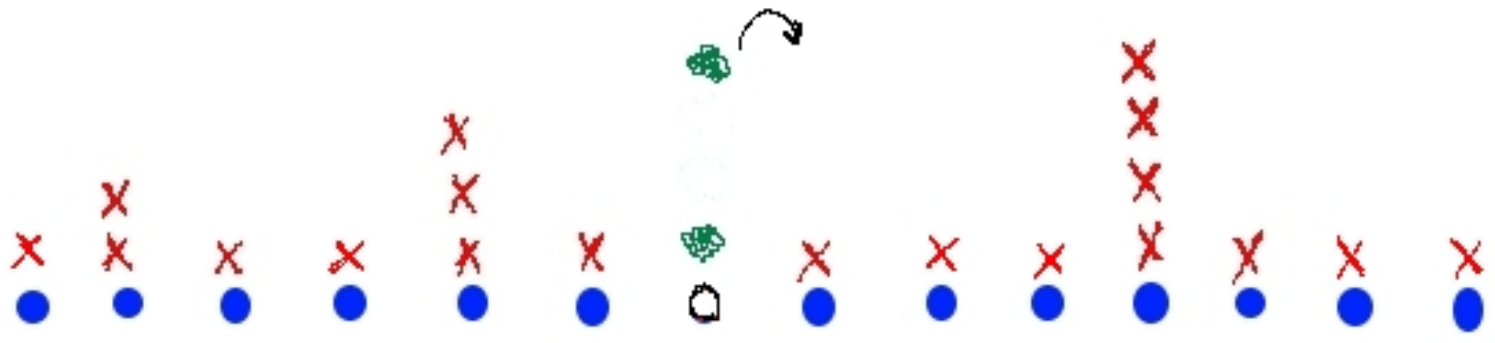

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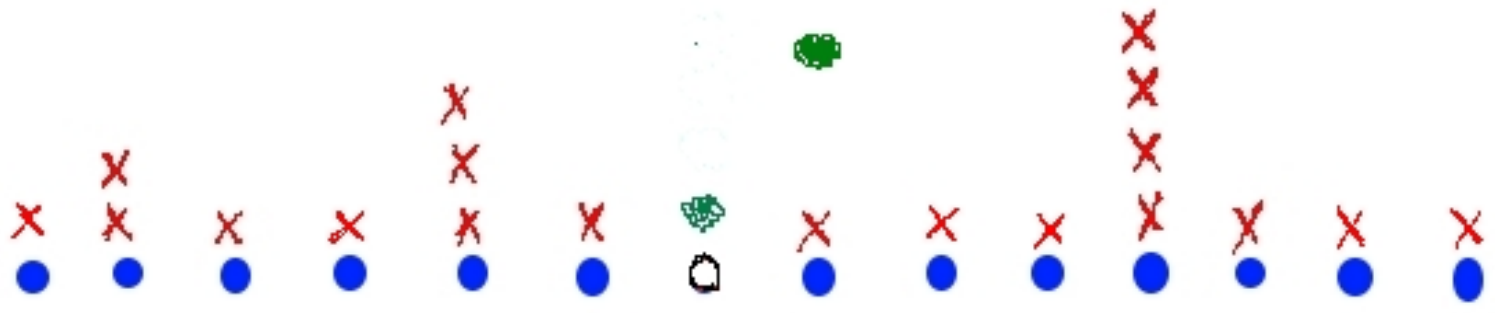

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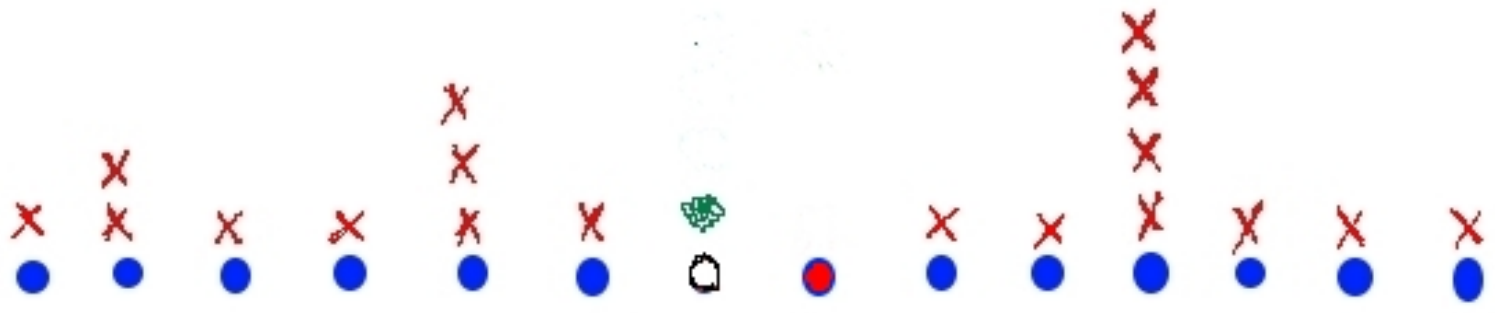

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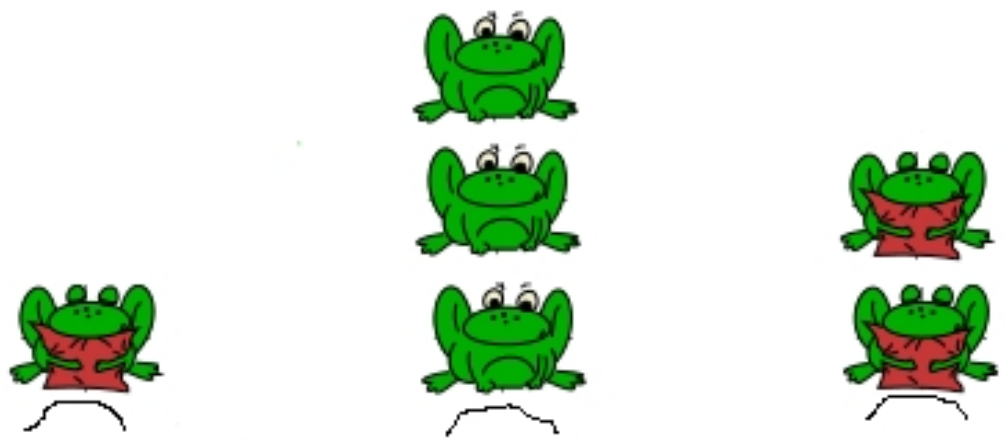
Under which conditions and **how fast**
pathogen populations spread in such a scenario?

Related work

- Sascha's poster!
- For host resistances of 1 the model is known as the **frog model**
  Each site of $\mathbb{Z}$ is interpreted as a stone. Initially on all stones frogs are sleeping (in our case the pathogens that potentially be generated at host infection). On the origin the frogs are waken up. They jump around according to symmetric, independent random walk. While jumping they wake up frogs on stones, where they are jumping on. Frogs do not die!



Modified figure: original figure by Felicitas Weidner

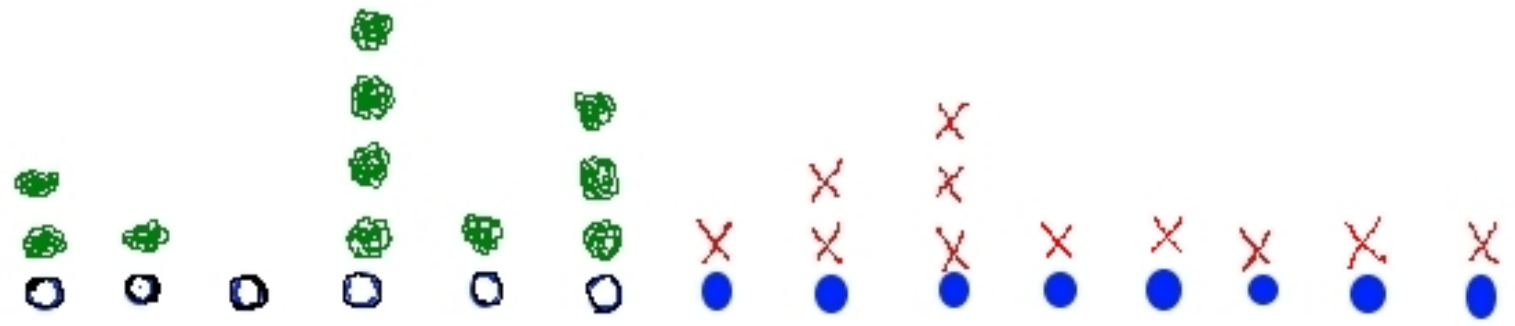
Related work

- For the frog model in $\mathbb{Z}^d$ a shape theorem is known, see Ramirez and Sidoravicius (2004), Comets, Quastel and Ramirez (2009).
- In the frog model with death frogs die after exponentially distributed time.
- Hoffmann, Johnson and Junge (2017) consider an infection model with host resistances. In this model pathogens do not die when infecting a resistant host, but just move further.

Assumptions

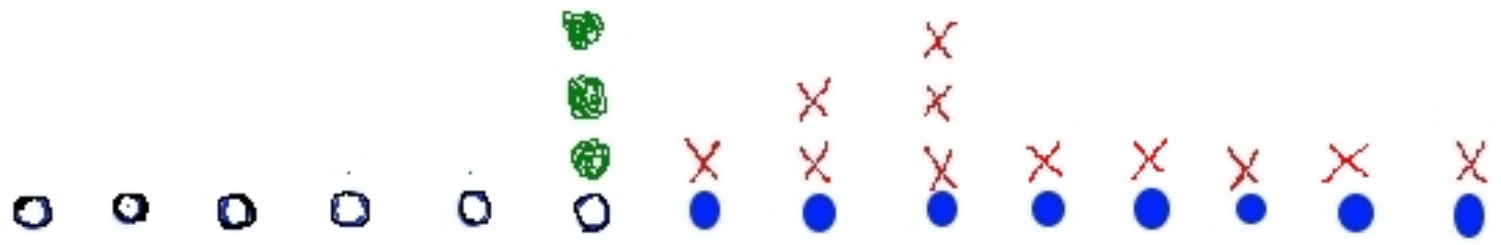
Initial pathogen distributions

- $\omega_{-\infty,1}$: infinite supply of pathogens left to the origin, hosts right to the origin
  - on each site x with $x \leq 0$ there are O_x pathogens, with $(O_x)_{x\leq 0}$ iid $\mathbb{N}_0$-valued, $O_x \sim O \leq o$ for some $o \in \mathbb{N}$.
  - one host on each site x with resistance R_x for $x \geq 1$ with $(R_x)_{x\geq 1}$ iid $\mathbb{N}$-valued



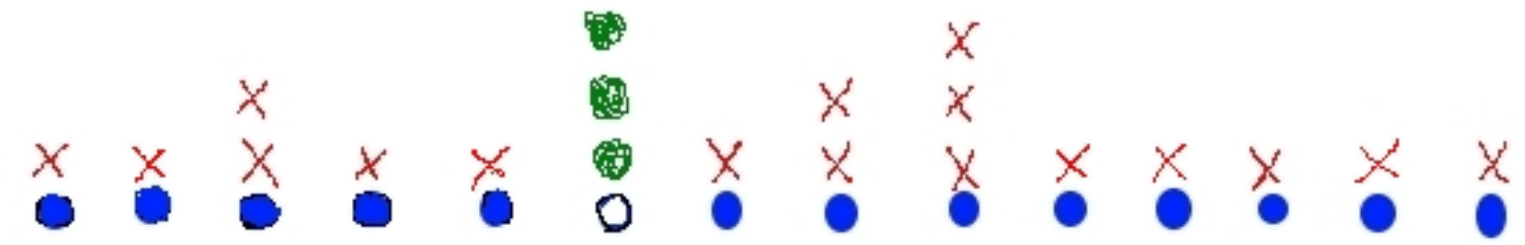
Initial pathogen distributions

- $\omega_{\delta_0,1}$: pathogens on site 0 seed the infection,
  hosts right to the origin
  - A_0 pathogens on site 0
  - no pathogens anywhere else
  - 1 host on each site x for $x \geq 1$ with resistance R_x for $x \geq 1$ with $(R_x)_{x \geq 0}$ iid $\mathbb{N}$-valued



Initial pathogen distributions

- $\omega_{\delta_0,2}$: pathogens on site 0 seed the infection, hosts on both sides of the origin
  - A_0 pathogens on site 0
  - no pathogens anywhere else
  - 1 host on each site x for $x \geq 1$ with resistance R_x for $x \neq 0$ with $(R_x)_{x \neq 0}$ iid $\mathbb{N}$-valued



Offspring pathogens

On sites k which are initially occupied by hosts pathogens can be generated.

- The offspring numbers $O_k \sim O$ are iid $\mathbb{N}_0$-valued.
  We assume $O \leq o$ for some $o \in \mathbb{N}$. In this case the process is well-defined and some calculations are simplified.

Interpretation of resistances

- $R \sim Geo(p)$ for some $p \in (0, 1)$. Infection history of a host does not influence susceptibility to the infection
- $R = c$: Certain resistance needs to be broken in a host
- R heavy-tailed distribution: Some hosts have a very high resistance to the infection
- In our model time between infection trials of a host does not influence the probability to be infected

Survival of pathogens

Under the initial condition

- $\omega_{-\infty,1}$ pathogens survive a.s.
- $\omega_{\delta_0,1}$ the survival probability is positive, if $\mathbb{E}[R] < \mathbb{E}[O]$.
- $\omega_{\delta_0,2}$ the survival probability is positive, if $\mathbb{E}[R] < \mathbb{E}[O]$ and $\mathbb{P}(R_{-1} + R_1 \leq O_0) > 0$ (or if $\mathbb{E}[R] < \mathbb{E}[O]$ and $\mathbb{E}[R^{2\alpha}] < \infty$ for some $\alpha > 3$).

Proof sketch for $\omega_{\delta_0,1}$

Assume $\mathbb{E}[R] < \mathbb{E}[O]$.

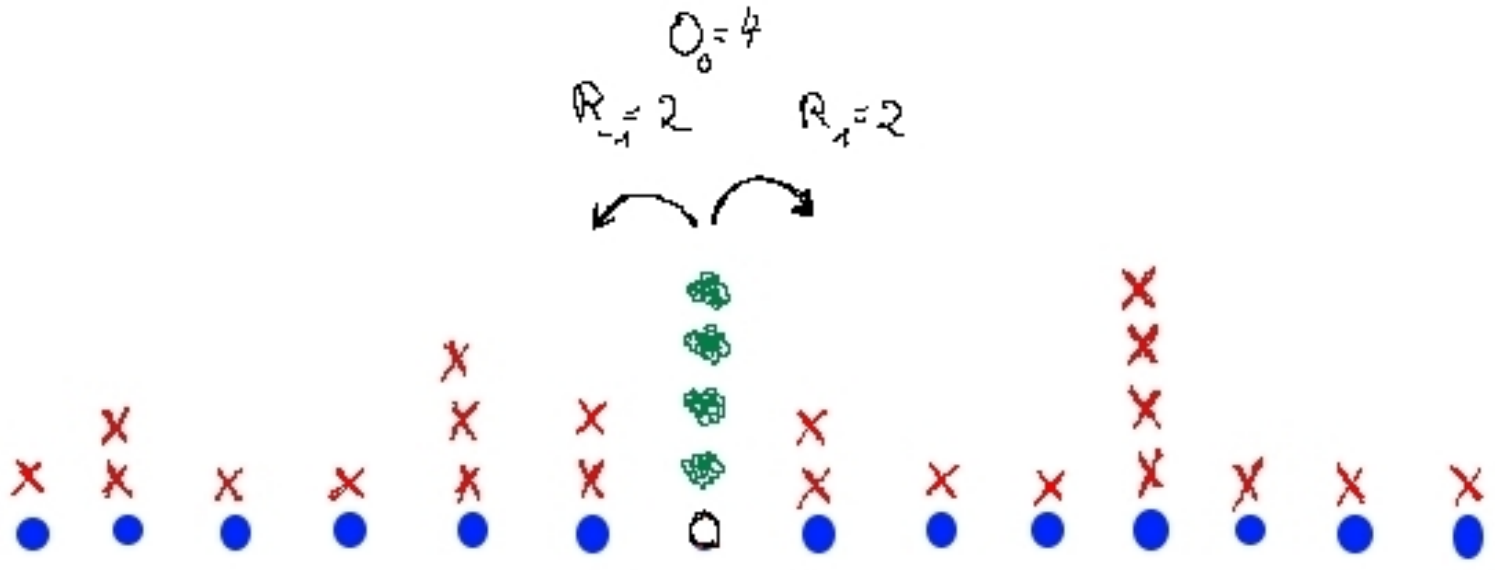
- Since random walks are recurrent on $\mathbb{Z}$,
  for survival hosts need to be infected one after the other.
- Since pathogens perform symmetric random walks and only the sites to the right need to be infected,
  survival is equivalent to the event

$$\bigcap_{n=1}^{\infty} \left\{ \sum_{k=1}^{n} R_k \leq \sum_{k=1}^{n} O_{k-1} \right\}.$$

  This event can be interpreted as the event that a random walk with step size distributed as $O - R$ stays non-negative.
  Since we assumed $\mathbb{E}[O] > \mathbb{E}[R]$, the random walk is transient with a drift towards ∞ and
  hence the survival probability is positive.

Proof sketch for $\omega_{\delta_0,2}$ under the assumption that $\mathbb{E}[R] < \mathbb{E}[O]$ and $\mathbb{P}(R_{-1} + R_1 \leq O_0) > 0$

- Consider a realisation with $R_{-1} + R_1 \leq O_0$. There are enough pathogens to infected the hosts on -1 and 1.
- Reenumerate the offspring numbers and the strengths of resistances generated at subsequent infection events according to the order they are occuring (and not by the site at which the correspondings hosts are located).



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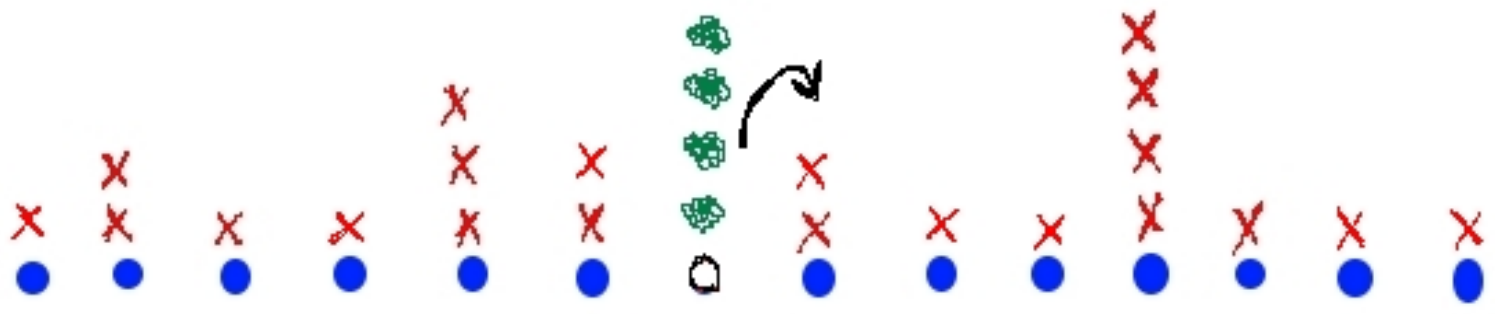

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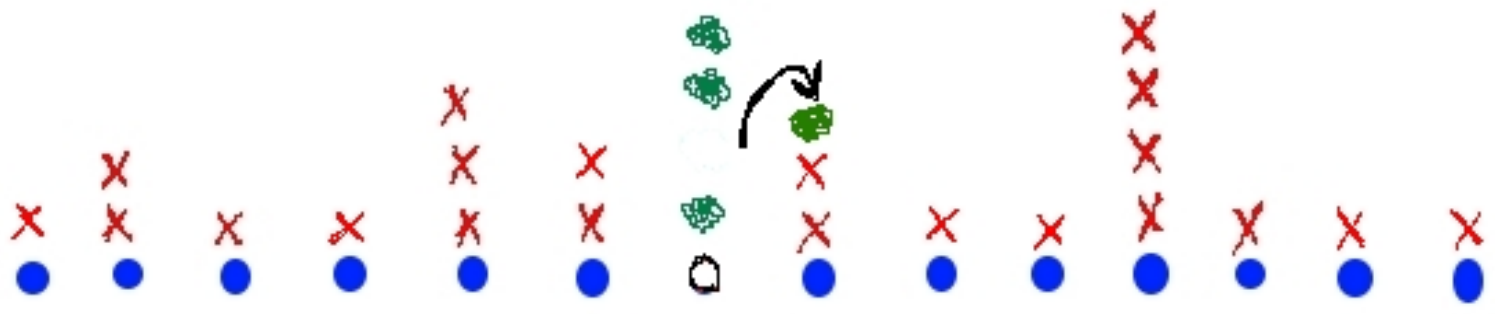

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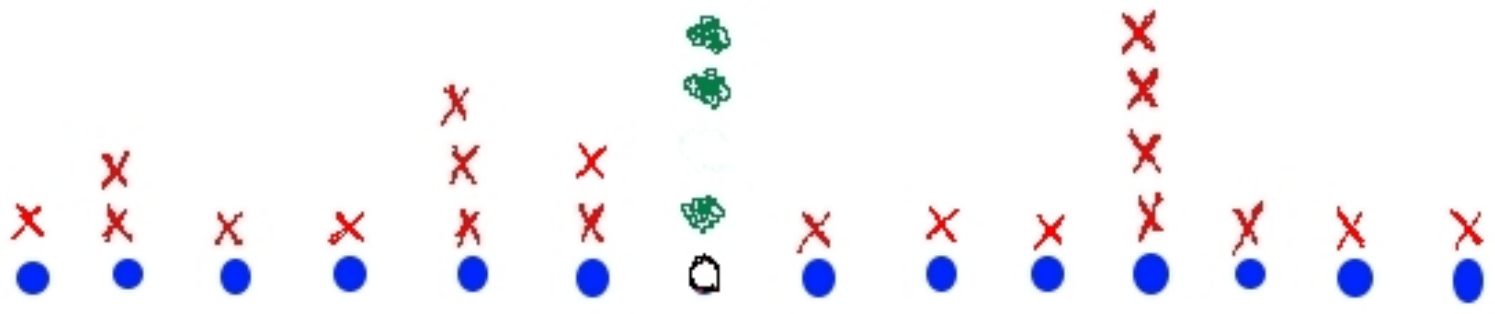

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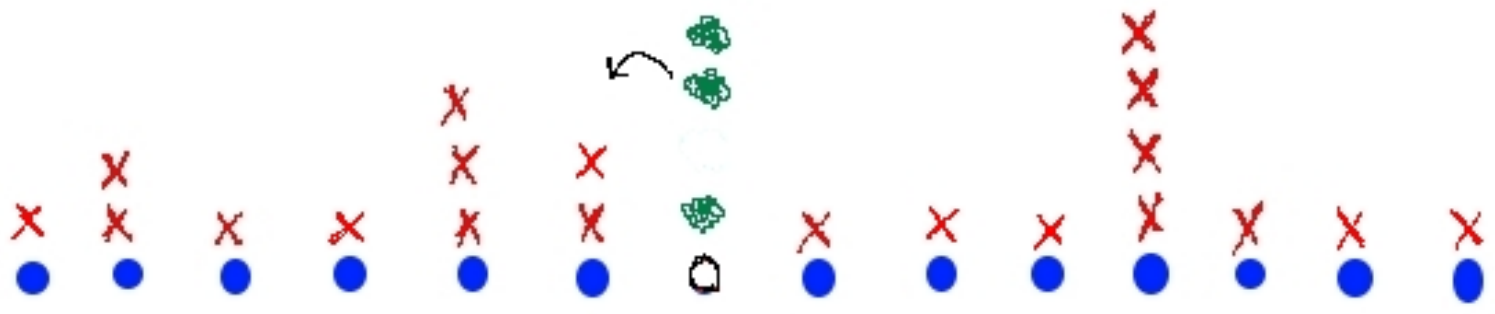

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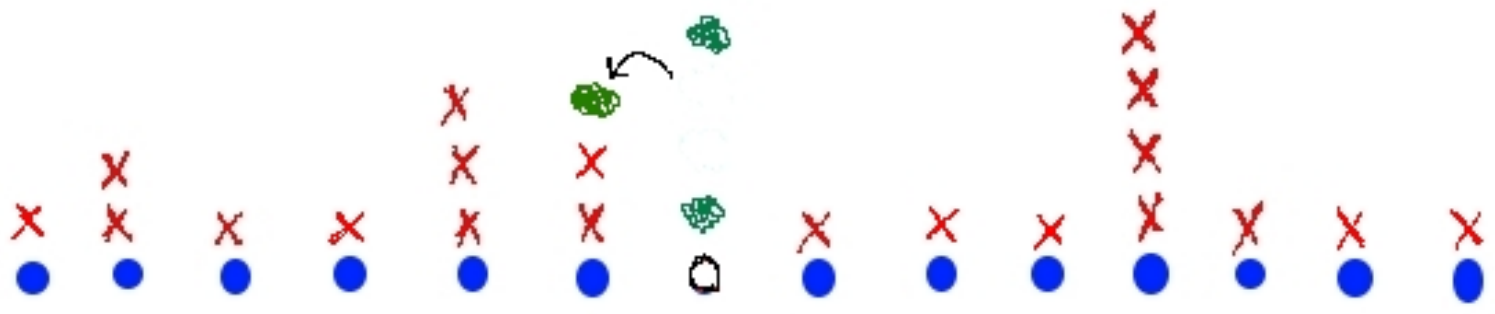

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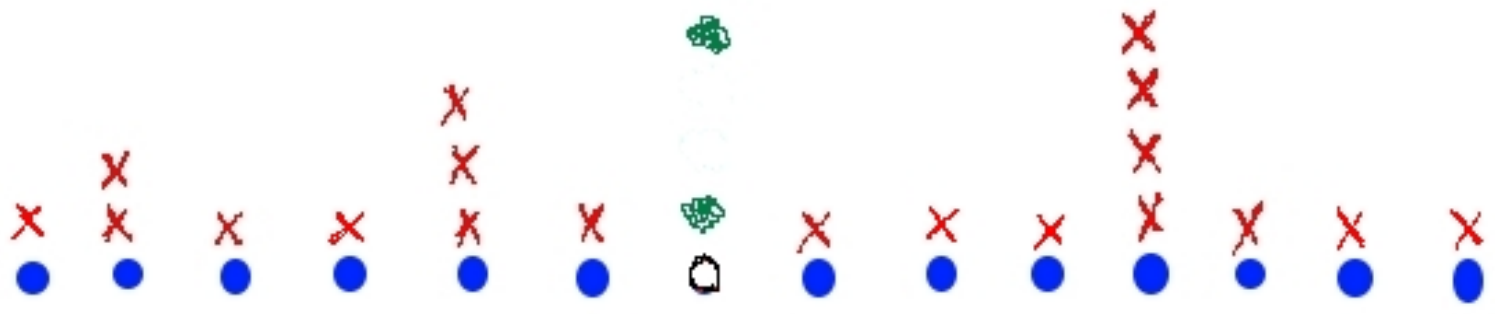

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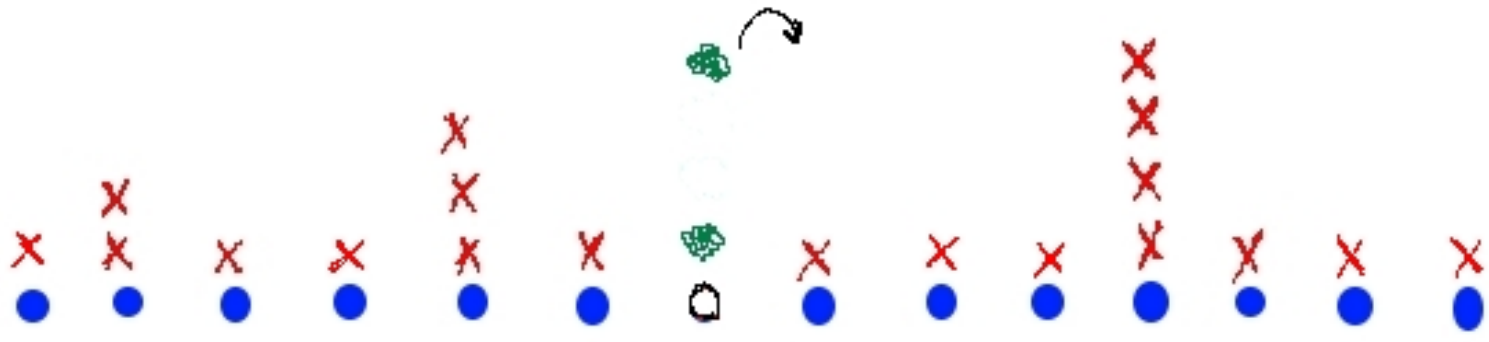

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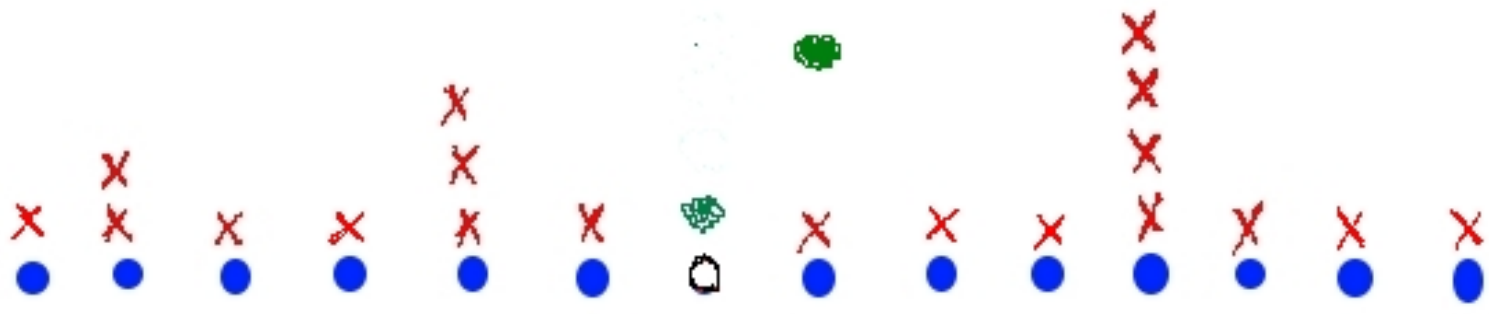

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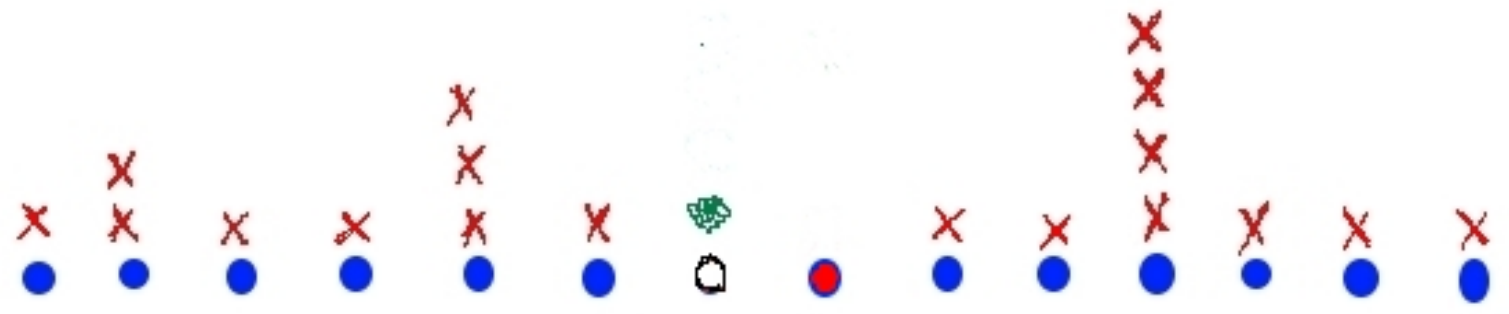

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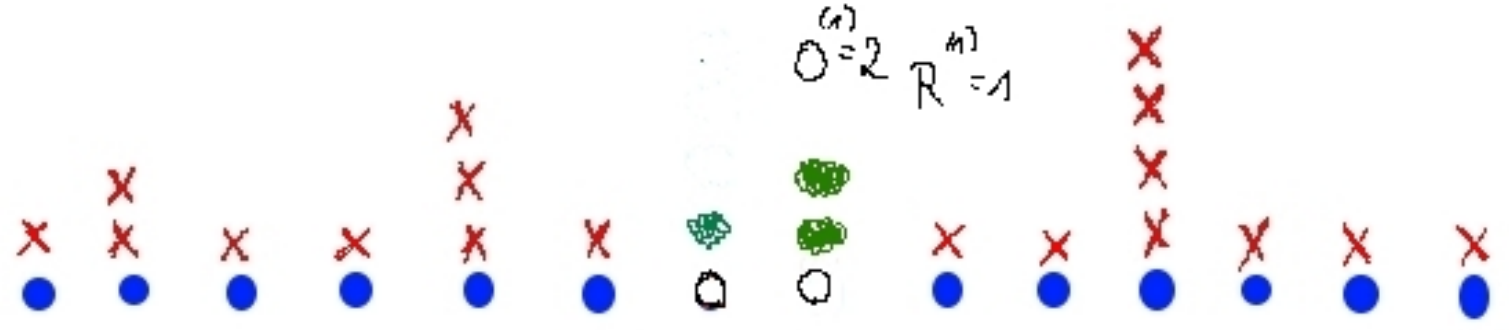

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- Reenumerate the offspring numbers and the strengths of resistances generated at subsequent infection events according to the order they are occuring (and not by the site at which the correspondings hosts are located). Then the pathogens survives, if

$$A = \cap_{n=1}^{\infty} \left\{ \sum_{k=1}^{n} R^{(k)} \leq \sum_{k=1}^{n} O^{(k)} \right\}$$

  happens. Since $\mathbb{E}[R] < \mathbb{E}[O]$, this event occurs with positive probability. As the event A is independent of the event $\{R_{-1} + R_1 \leq O_0\}$.

Spread of infection (weak conditions)

Consider the initial conditions $\omega_{-\infty,1}$ and $\omega_{\delta_0,1}$.
Let r_t be the rightmost infected site at time t.
Assume $\mathbb{E}[R^{2\alpha}] < \infty$ for some $\alpha > 1$, then there exist $C_1, C_2 \in (0, \infty)$, such that conditioned on survival

$$C_1 \leq \liminf_{t\to\infty} \frac{r_t}{t} \leq \limsup_{t\to\infty} \frac{r_t}{t} \leq C_2 \quad a.s.$$

Spread of infection (strong conditions)

Assume one of the following conditions is fulfilled:

- $\mathbb{E}[R^{2\alpha}] < \infty$ for some $\alpha > 5$ and $\mathbb{P}(O - R \geq 4) > 0$
- $\mathbb{E}[R^{2\alpha}] < \infty$ for some $\alpha \in (2 + \sqrt{5}, 5]$ and $\mathbb{P}(O - R \geq 5) > 0$.

Then there exists a $\gamma \in (0, \infty)$ such that conditioned on survival almost surely under the initial conditions $\omega_{-\infty,1}$, $\omega_{\delta_0,1}$ and $\omega_{\delta_0,2}$

$$\lim_{t\to\infty} \frac{r_t}{t} = \gamma$$

and under $\omega_{\delta_0,2}$ in addition for the leftmost site ℓ_t it holds a.s.

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Spread of infection (strong conditions)

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These conditions are only sufficient, but not necessary, because e.g for the frog model with $O \equiv 2$ and $R \equiv 1$ and the spread is also linear.

Proof sketches

Spread of infection (weak conditions)

Consider the initial conditions $\omega_{-\infty,1}$ and $\omega_{\delta_0,1}$ and.
Let r_t be the rightmost infected site at time t.
Assume $\mathbb{E}[R^c] < \infty$ for some $c > 2$, then there exist $C_1, C_2 \in (0, \infty)$, such that conditioned on survival

$$C_1 \leq \liminf_{t\to\infty} \frac{r_t}{t} \leq \limsup_{t\to\infty} \frac{r_t}{t} \leq C_2 \quad a.s.$$

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Consider first the initial condition $\omega_{-\infty,1}$

Upper bound

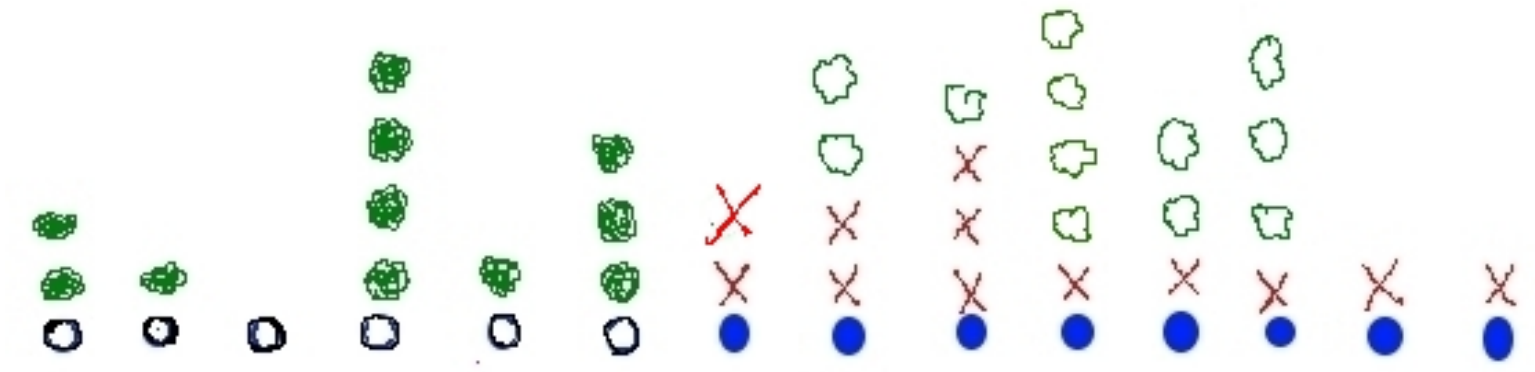
- $\mathbb{E}[O] > \mathbb{E}[R]$: Supercritical regime
- Coupling with a branching random walk where hosts do not resist yields an upper bound

Lower bound

- Controll resistances to construct an auxiliary process which moves not faster than the original process

Lower bound: Controlling resistances

- Finding regions of "good resistances and good offspring numbers" with hosts having enough offspring to compensate for the loss at host resistance and to push the front forward fast enough
  Moment conditions on resistances guarantee, that for each site with high enough probability we do not need to consider a too large region next to the site



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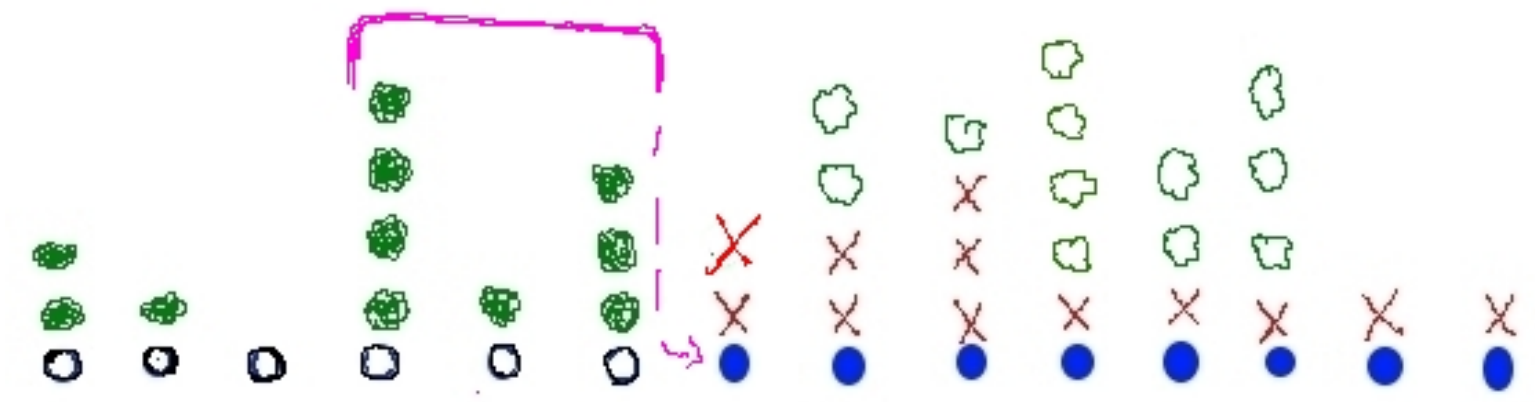

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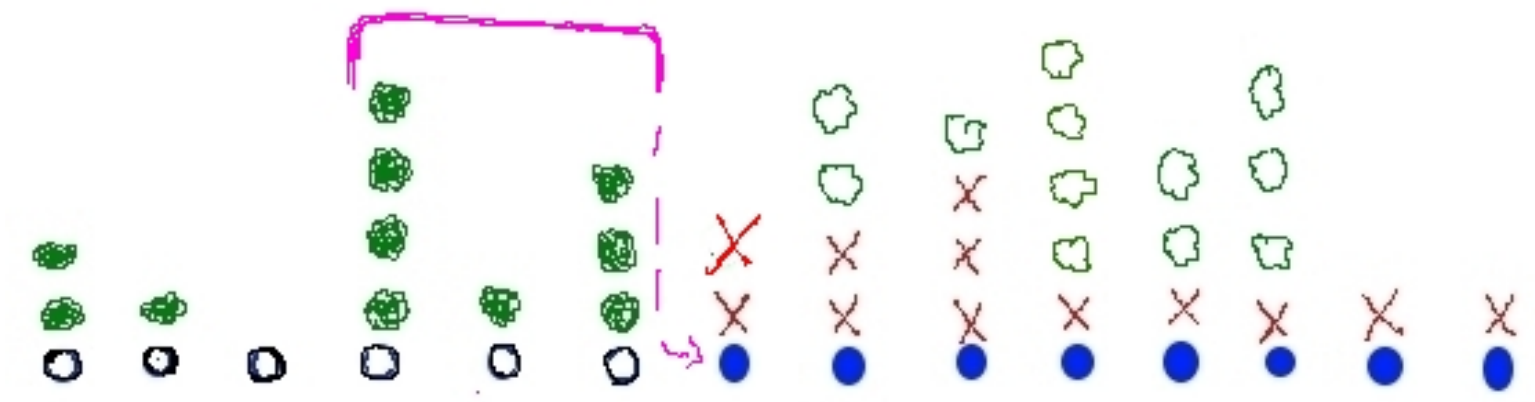

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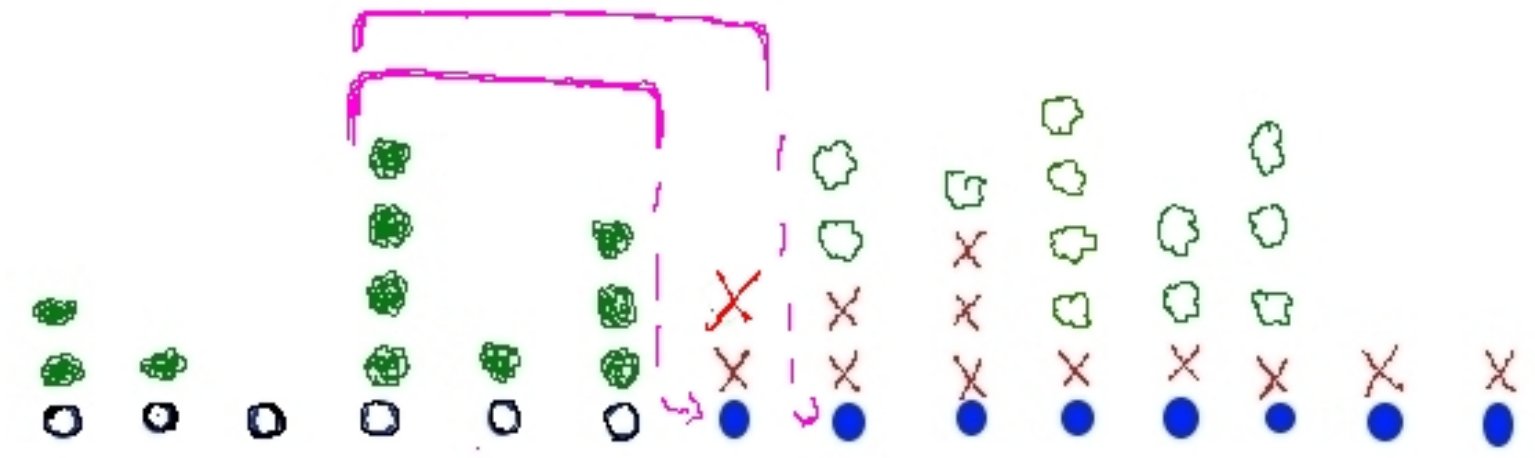

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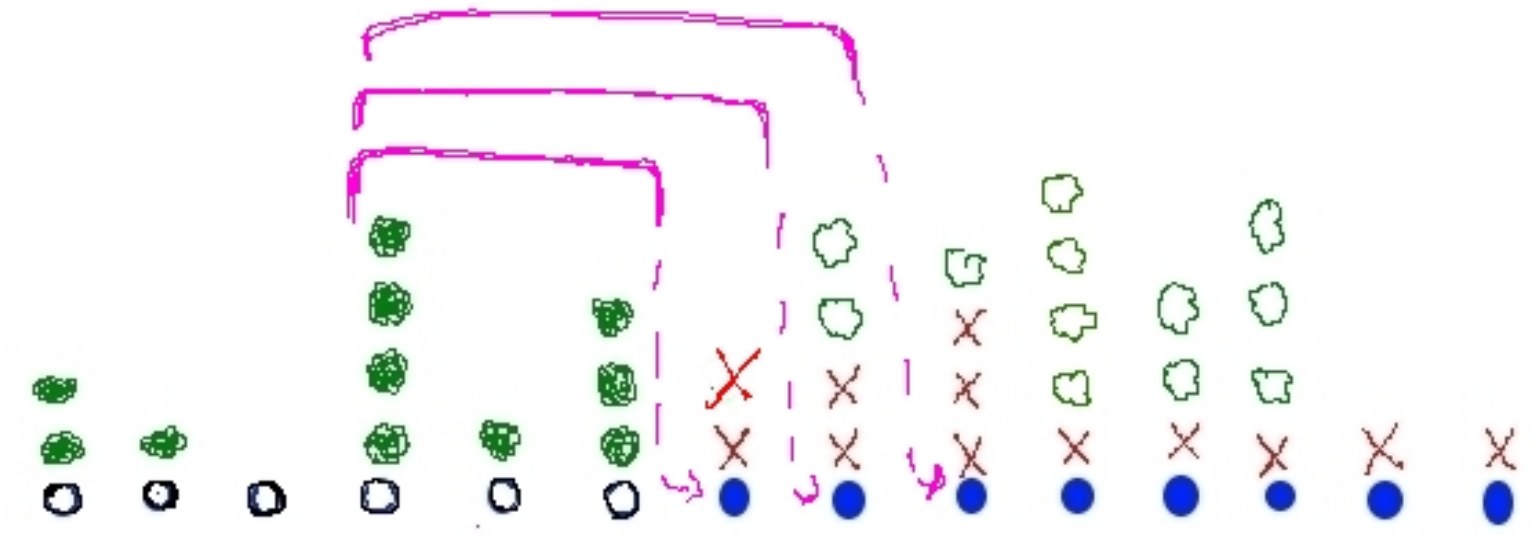

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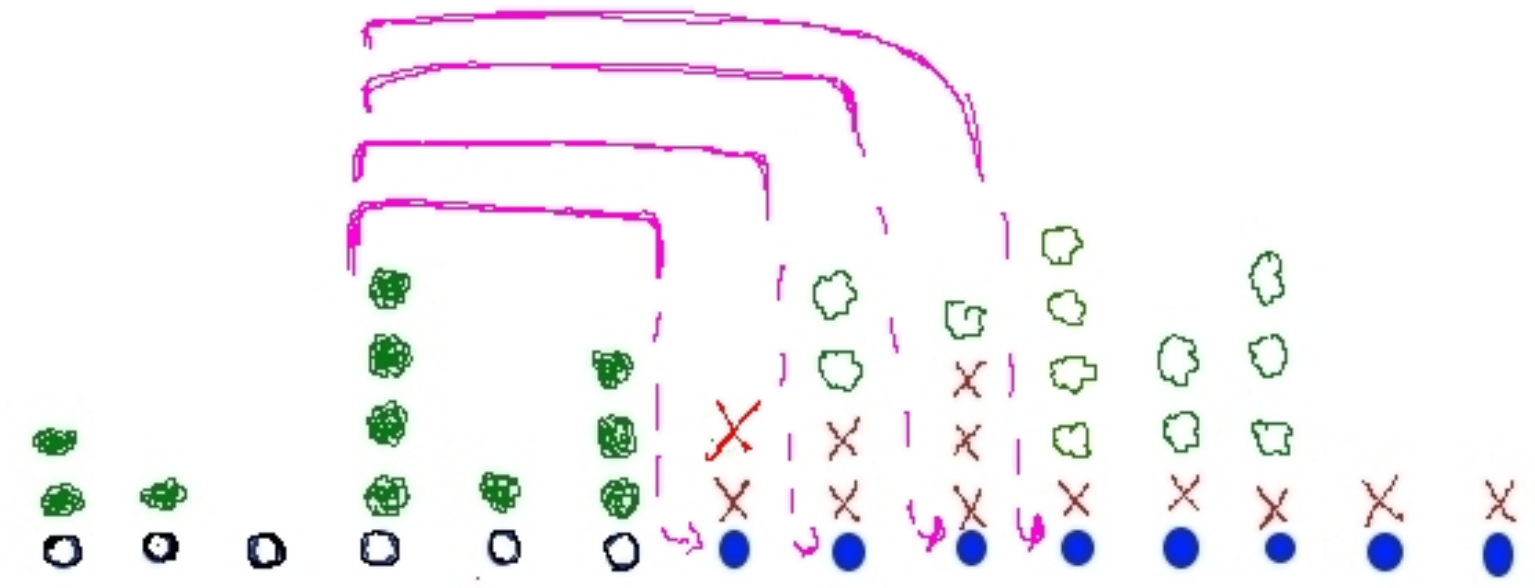

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  Moment conditions on resistances guarantee, that for each site with high enough probability we do not need to consider a too large region next to the site.
- Using these regions we construct a sequence of waiting times $(\nu_n)_{n\in\mathbb{N}}$ with
  - ν_n upper bounds the time to move from $n-1$ to n consider only viral particles born in the good region
  - ν_n identically distributed
  - $\nu_n \in L^q$ for all $1 \leq q < \frac{\alpha+1}{2}$
  - $(\nu_n)_{n\in\mathbb{N}}$ is stationary and a ϕ-mixing sequence with $\phi(n) = \mathcal{O}(n^{-\frac{1}{2}+\varepsilon})$, because the size of good regions is not too large
- Birkhoffs pointwise ergodic theorem yields the lower bound.

Extending the technique for the initial condition $\omega_{\delta_0,1}$

Need to cope with

- conditioning on survival: Controll influence on particle movement
- no supply of viral particles left to the origin

Extending the technique for the initial condition $\omega_{\delta_0,1}$

- Find a site L (with finite distance to the origin) from which on offspring numbers can well compensate resistances,
  more precisely for all $n \geq L$
  $\sum_{k=1}^{n} R_{L+k-1} \leq \beta_R n$ and $\sum_{k=1}^{n} O_{L+k} \geq \beta_O n$
  for appropriate $\beta_R < \beta_O$
- Show conditioned on surival $L < \infty$ a.s. and the time to reach site L is a.s. finite
- Starting from L on we build waiting times $(\tilde{\nu}_n)_{n \geq L}$ which give a lower bound on the times to move the front from $n-1$ to n similar as the waiting time $(\nu_n)_{n \in \mathbb{N}}$ for $\omega_{-\infty,1}$
- Show that $\tilde{\nu}_n \in L^q$ and $(\tilde{\nu}_n)_{n \geq L}$ are ϕ-mixing with
  $\phi(n) \in \mathcal{O}(n^{-c/2+\varepsilon})$
- Furthermore $(\tilde{\nu}_n)_{n \geq L}$ is asymptotically distributed as $(\nu_n)_{n \geq 1}$
- SLLN for L^q-mixingales yields the claim, see Serfling (1968).

Spread of infection (strong conditions)

Assume one of the following conditions is fulfilled:

- $\mathbb{E}[R^c] < \infty$ for some $c > 10$ and $\mathbb{P}(O - R \geq 4) > 0$
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and under $\omega_{\delta_0,2}$ in addition for the leftmost site ℓ_t it holds a.s.

$$\lim_{t\to\infty} \frac{\ell_t}{t} = -\gamma.$$

Proof sketch

- The conditions guarantee a positive survival probability also for $\omega_{\delta_0,2}$. Use similar techniques as in the previous proof to show that with positive probability pathogens on the left do not help pathogens to spread on the right and vice-versa.
- Use subadditivity arguments to show almost sure convergence
- Identify a sequence of subsequent sites $(M^i)_{i\geq 0}$ from each of which on offspring numbers can well compensate for resistances.
- Show that subsequent sites are not too far from each other and the distance $M^i - M^{i-1}$ are identically distributed for $i \geq 1$.
- Let T_i be the time to reach site M^i
- Show that the distribution functions of the times $T_i - T_0$ fulfill a subadditivity property, have second moments and $T_0 < \infty$ a.s.
- The claimed result follows then by subadditivity, see Smythe, Wierman (1987) based on a result by Hammersley (1974).

Thank you!

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