Branching model for proliferating parasites in dividing cells.

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4th Cornell Probability Summer School.

Motivations

To model cell division with parasite infection (more generally multiplication and sharing of cells' biological content such as proteins, mitochondrias).

To take into account unequal sharing of parasites, observed in experiments for bacteriophage lysogen in E-Coli (TaMaRa's laboratory-Hopital Necker, Paris).

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Binomial sharing of parasites.

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Equal sharing : $p = 1/2$.

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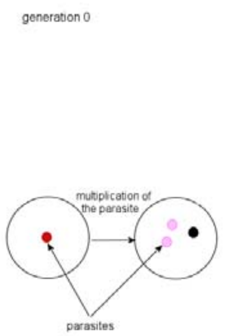

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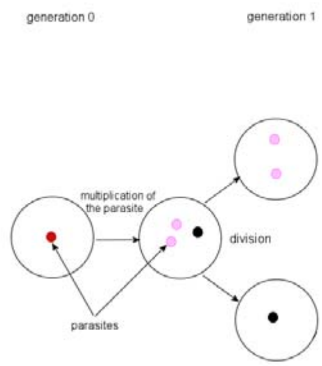

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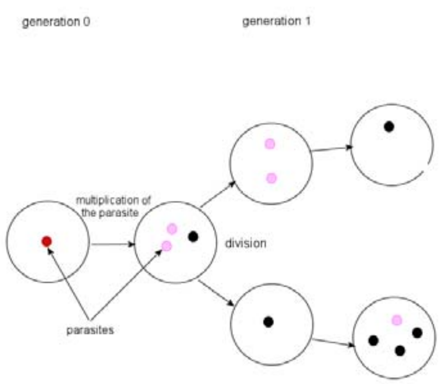

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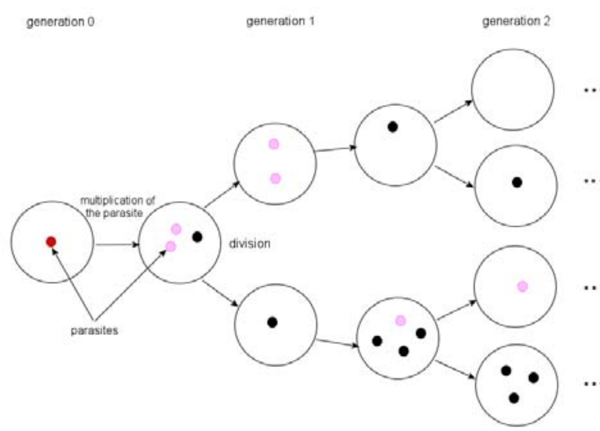
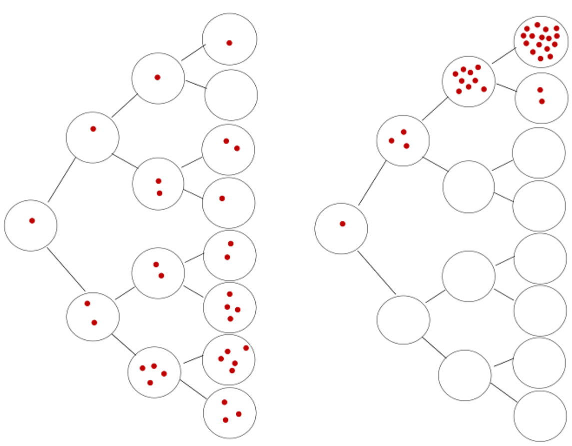


Equal/Unequal sharing



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Conditionally on $Z_{\mathbf{i}} = x$, the numbers of parasites of the daughter cells $(Z_{\mathbf{i}0}, Z_{\mathbf{i}1})$ are distributed as

$$\sum_{k=1}^{x}(Z_k^{(0)}, Z_k^{(1)}),$$

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$$m_0 := \mathbb{E}(Z^{(0)}), \qquad m_1 := \mathbb{E}(Z^{(1)}).$$

m_0 (resp. m_1) is the mean size of the offspring of a parasite which goes in the first (resp. second) daughter cell

Previously...

- Kimmel has considered the continuous version of this model (cells' life time is exponential) in the case

$$(Z^{(0)}, Z^{(1)}) \stackrel{d}{=} (Z^{(1)}, Z^{(0)}), \qquad \mathbb{E}(Z^{(0)}) = m_0 \in]1/2, 1[.$$

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- Guyon allows asymmetry and dependence but hypothesis and statements are different here.

Total number of parasites.

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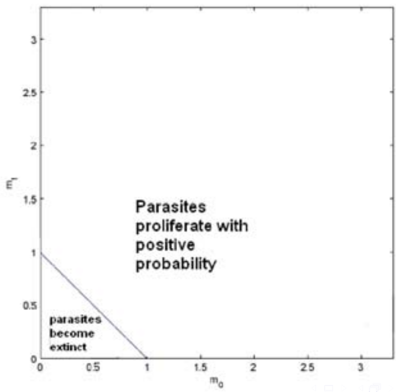

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- Here :
Population of parasites in a random cell line. Two equiprobable environments with resp. reproduction law $Z^{(0)}$ and $Z^{(1)}$.
$\Longrightarrow$ Criteria for a.s. extinction of the number of parasites along a random cell line : $m_0 m_1 \leq 1$.

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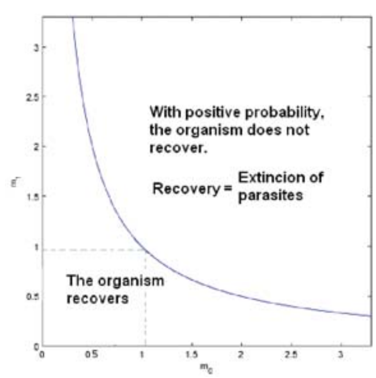

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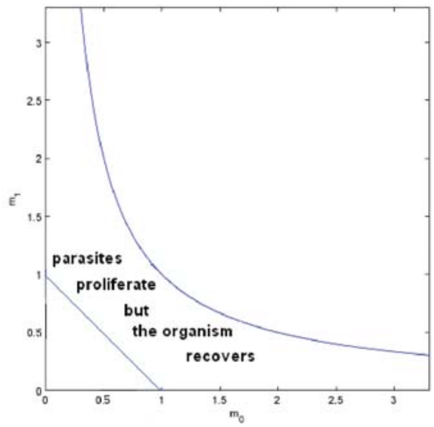

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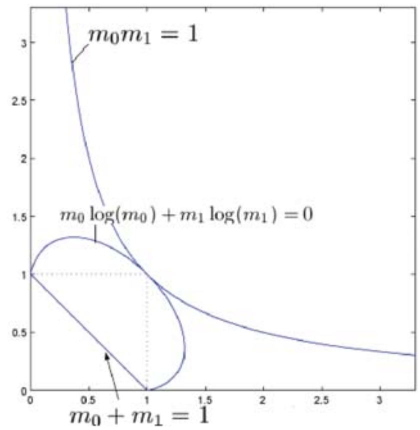
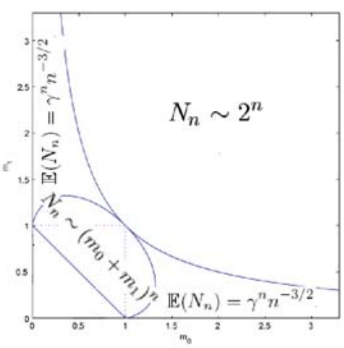


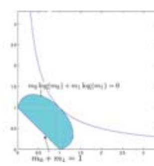
Asymptotic for the number of infected cells.

$N_n =$ Number of infected cells in generation n.



NB : $N_n \sim c_n$ means that N_n/c_n converges in probability to a finite positive random variable.

Asymptotic proportion of infected cells



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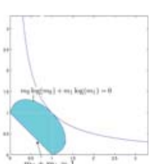

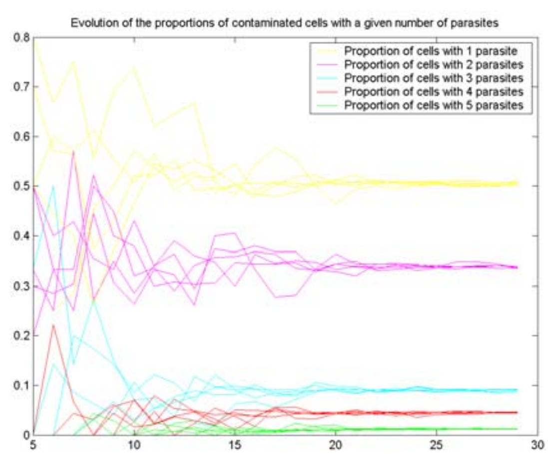

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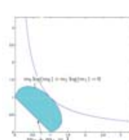

Theorem

Conditionally on non extinction of parasites,
Proportion of infected cells with k parasites $\overset{n\to\infty}{\longrightarrow} \mathbb{P}(\Upsilon = k)$.

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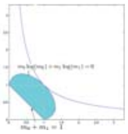

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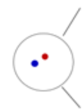
The convergence holds in probability.
Υ is the quasi stationary Yaglom distribution of the number of parasites in a random cell line Z_n (that it the limit distribution of Z_n conditioned to be positive).
Its probability generating function G is characterized by

$$G(f_0(s)) + G(f_1(s)) = (m_0 + m_1)G(s) + (2 - (m_0 + m_1)).$$

Separation of descendances of parasites.



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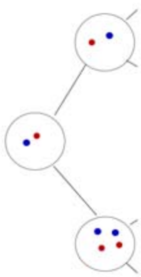

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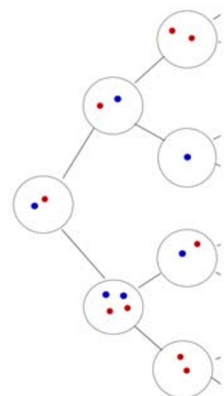

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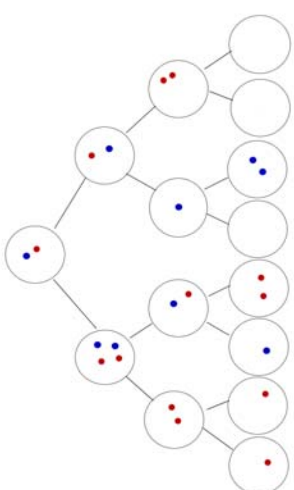

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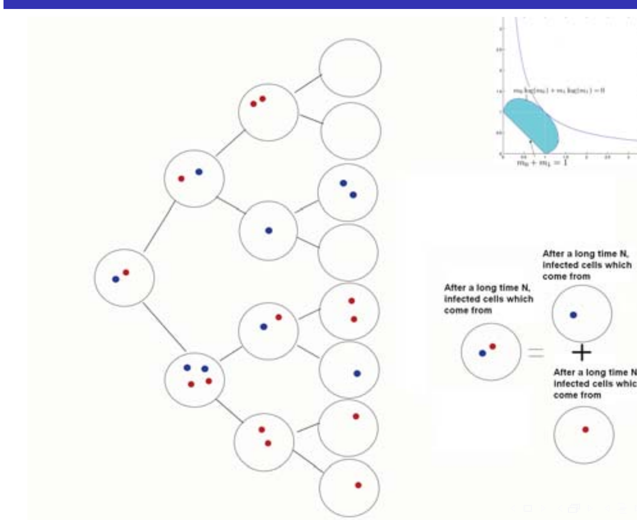

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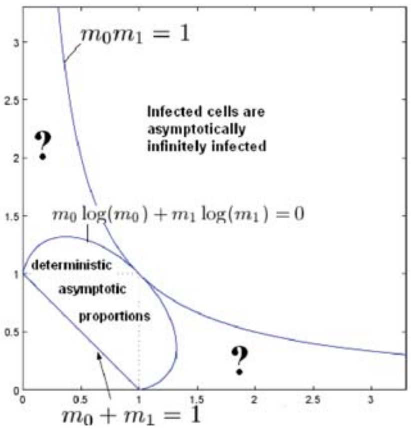
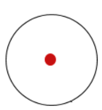


Cell division with contamination

We add now random contamination of cells by parasites which do not belong to the cell population, which depends on whether the cell is already infected or not.

Cell division with contamination

generation 0



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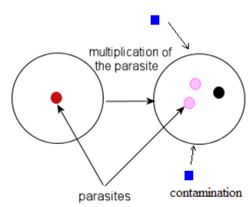

Cell division with contamination

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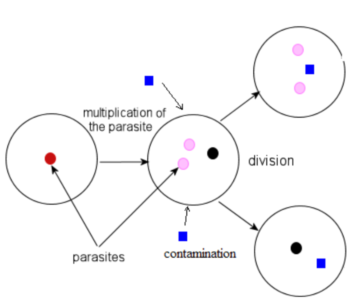

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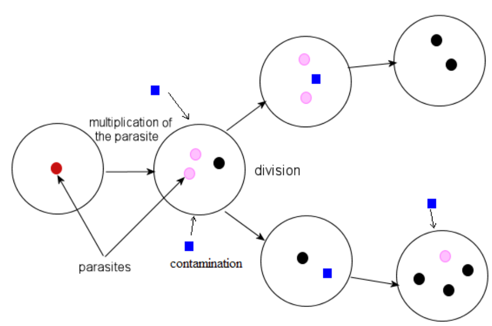

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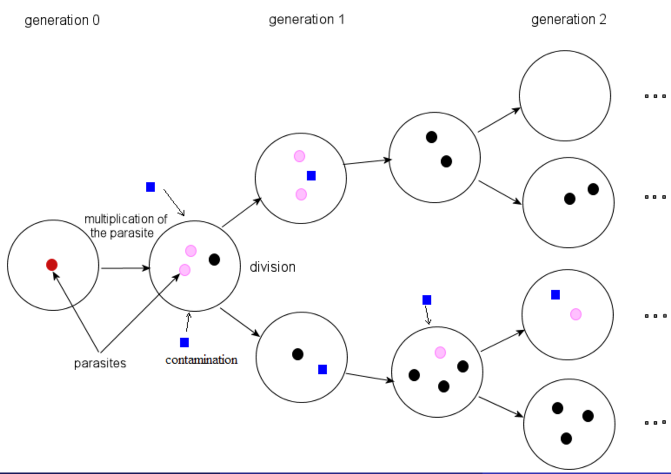

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$F_k(n)$ =Proportions of cells with k parasites in generation n.

Theorem

If $m_0 m_1 < 1$ and $\max(\mathbb{E}(\log^+(Y_i)) : i = 0, 1) < \infty$, then for every $k \in \mathbb{N}$, $F_k(n)$ converges in probability to a deterministic number f_k as $n \to \infty$, such that $\sum_{k=0}^{\infty} f_k = 1$.

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Otherwise, for every $k \in \mathbb{N}$, $F_k(n)$ converges in probability to 0 as $n \to \infty$.