Luria-Delbrück distribution 1943

Bacteria can mutate from virus sensitive to virus resistent.

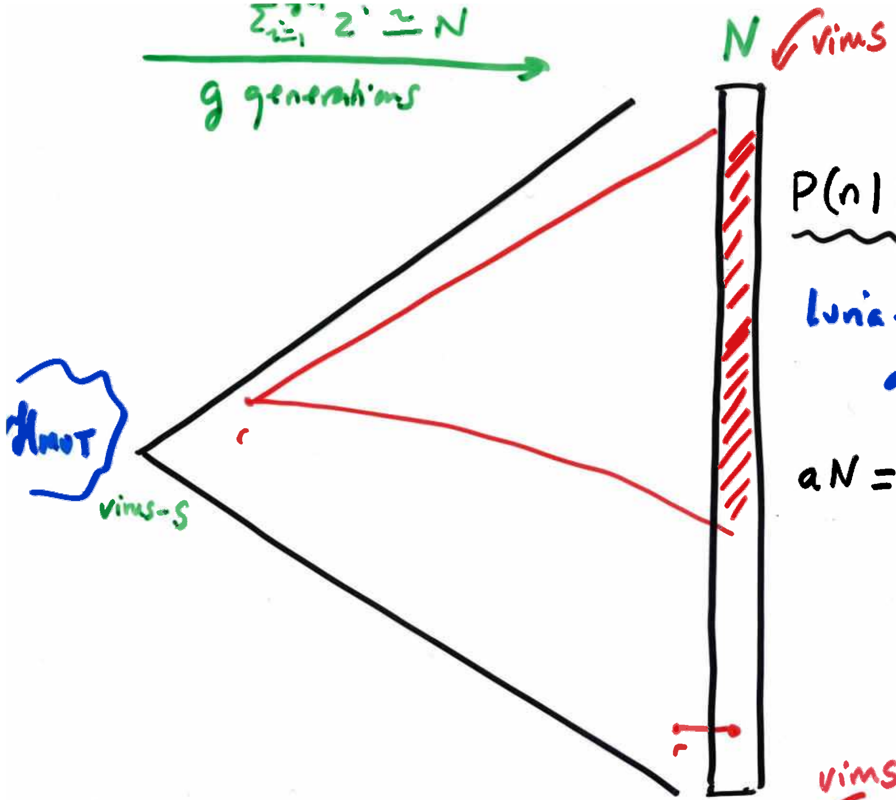
MUTATION $\mathcal{H}_1$: there is a finite probability "a" that a bacterium could mutate from virus-s to virus-r

INMUNITY $\mathcal{H}_0$: there is a finite probability "p" of a bacterium to survive the attack of a virus

They grew many ($N \cong 20$) identical cultures to

i) compare $\mathcal{H}_{mut}$ - $\mathcal{H}_{inmunity}$

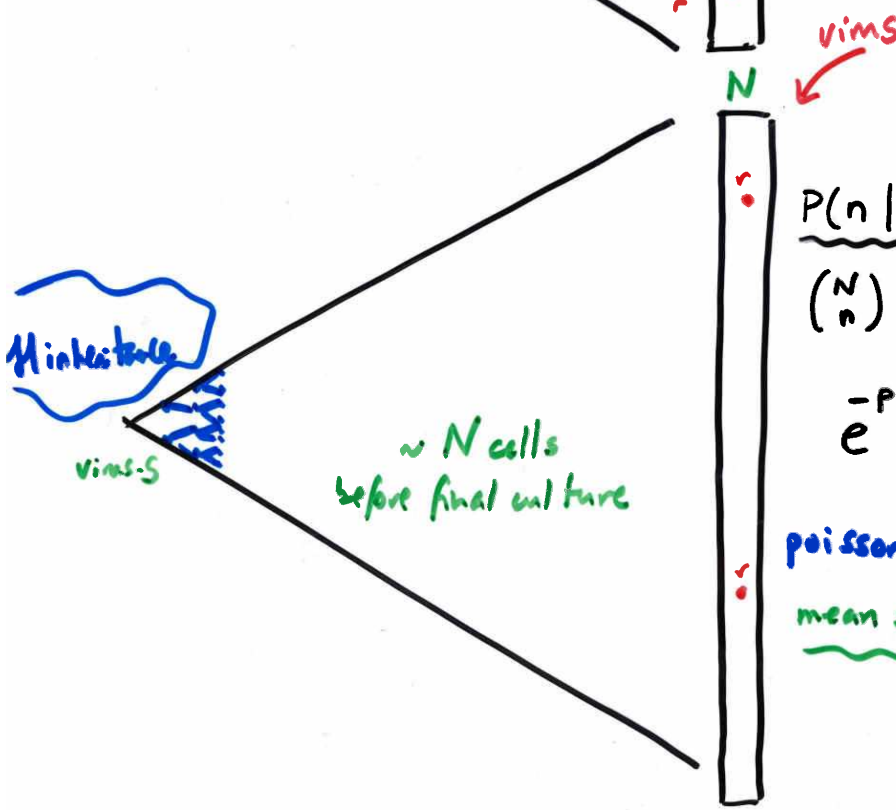
ii) estimate the rate of mutation from data.



$P(n \mid N, \mathcal{H}_{mutation}) =$

Luria-Delbrück distribution

aN = expected # of bacteria that become resistant



$P(n \mid N, \mathcal{H}_{inheritance}) =$

$$\binom{N}{n} p^n (1-p)^N \sim$$

$$e^{-pN} \frac{(pN)^n}{n!}$$

poisson distribution

mean = variance = pN

The fluctuation test

experiment #	16	21a
# cultures	20	19
culture		
1	1	0
2	0	0
3	3	0
4	0	0
5	0	8
6	5	1
7	0	0
8	5	1
9	0	0
10	6	15
11	107	0
12	0	0
13	0	19
14	0	0
15	1	0
16	0	17
17	0	11
18	64	0
19	0	0
20	35	
MEAN	11.35	3.8
VARIANCE	694	40.8

We reject the "acquired immunity" hypothesis

Estimation of mutation probability

they used 2 methods.

One based on the average # of resistant bacteria gets it pretty wrong

$$a \approx 2.45 \cdot 10^{-8}$$

because the distribution has a very heavy tail and large variances

(culture sizes $\simeq 10^{8}$)

Think bayesian

data : M experiments

$\frac{n_i}{N}$ mutated bacteria for exp $i = 1, \dots, M$

$(n = \sum_{i=1}^{M} n_i)$

parameters : a probability of a mutation

unknown : r # of mutated bacteria, $\langle r \rangle = aN$

$$\boxed{P(n \mid M, N, a)} =$$

$$= \sum_{r=1}^{N} P(n \mid r)\, P(r \mid a)$$

a poisson

$$e^{-aN} \frac{(aN)^r}{r!}$$

$$\boxed{\simeq \left(e^{-aN}\right)^{m_0} \left(1 - e^{-aN}\right)^{M - m_0}}$$

(m_0 = # exp without resistant bacteria)

* Posterior distribution for a

$$\underbrace{\left(e^{-aN}\right)^{m_0}\left(1-e^{-aN}\right)^{M-m_0}}$$

$$M = 20$$
$$m_0 = 11$$
$$N = 5.6 \times 10^{8}$$

Confidence Interval to cover 95% of distribution

$$a = \left(0.56 \cdot 10^{-9},\ 2.07 \cdot 10^{-9}\right)$$

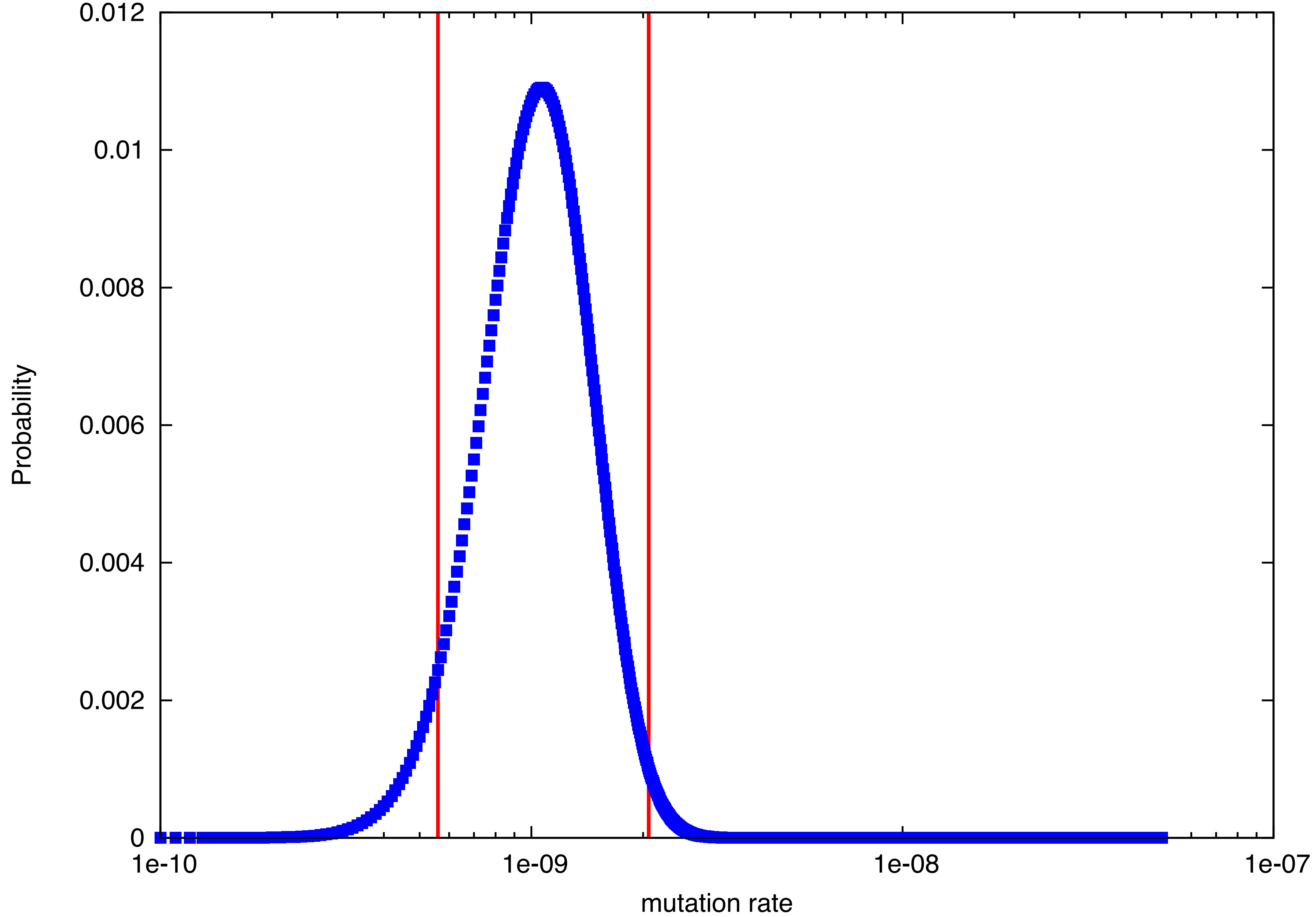
* Model comparison:

$$P(\text{data} \mid H_{\text{mut}}) = \int_0^1 da \left(e^{-aN}\right)^{m_0}\left(1-e^{-aN}\right)^{M-m_0}$$

$$P(\text{data} \mid H_{\text{immunity}}) = \int_0^1 dp \left(e^{-pN}\right)^{M} \frac{(pN)^{\sum_i n_i}}{n_1! \cdots n_M!}$$

then $$\frac{P(\text{data} \mid H_{\text{mut}})}{P(\text{data} \mid H_{\text{immunity}})} \simeq e^{372.0}$$

Luria-Delbruck distribution



Sum up

Bayesian inference good for

i) model comparison

ii) estimation of parameters

o) stating the assumptions of the inference

iii) Models are probabilistic, thus give a **DIRECT** chance to asses the validity of the model to describe your observations by **sampling**