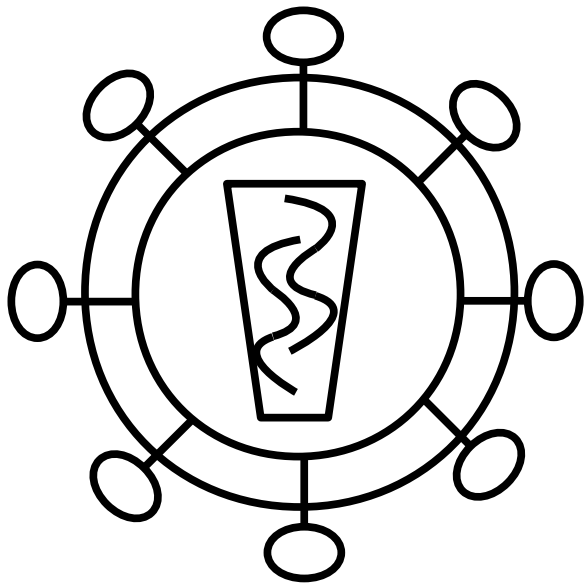


# Selective sweeps in HIV



Pleuni Pennings  
Sergey Kryazhimskiy  
John Wakeley

Harvard University



# Take home message

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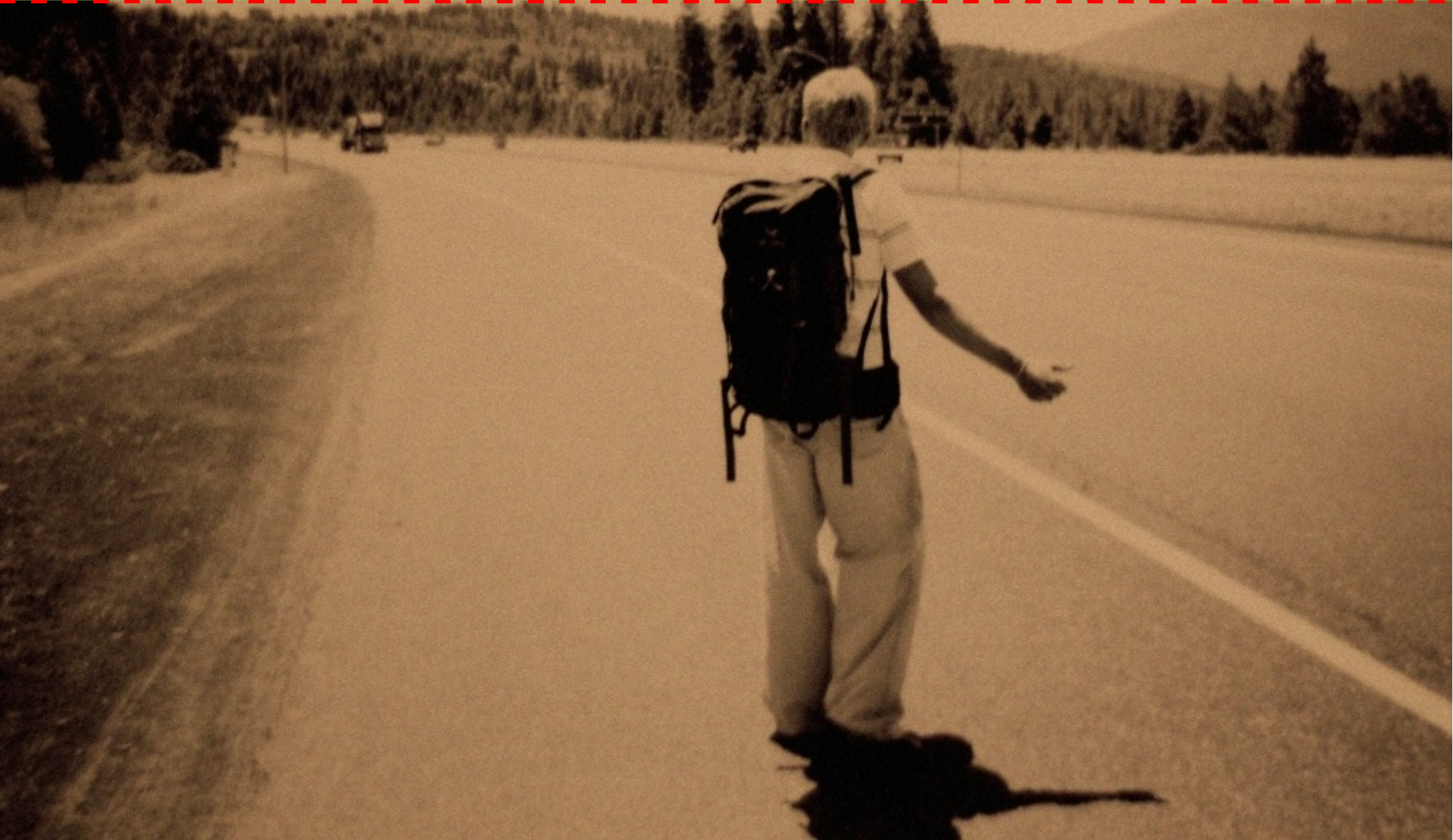
1. Sweeps occur in HIV
2. Nonsynonymous sites recover faster than synonymous sites



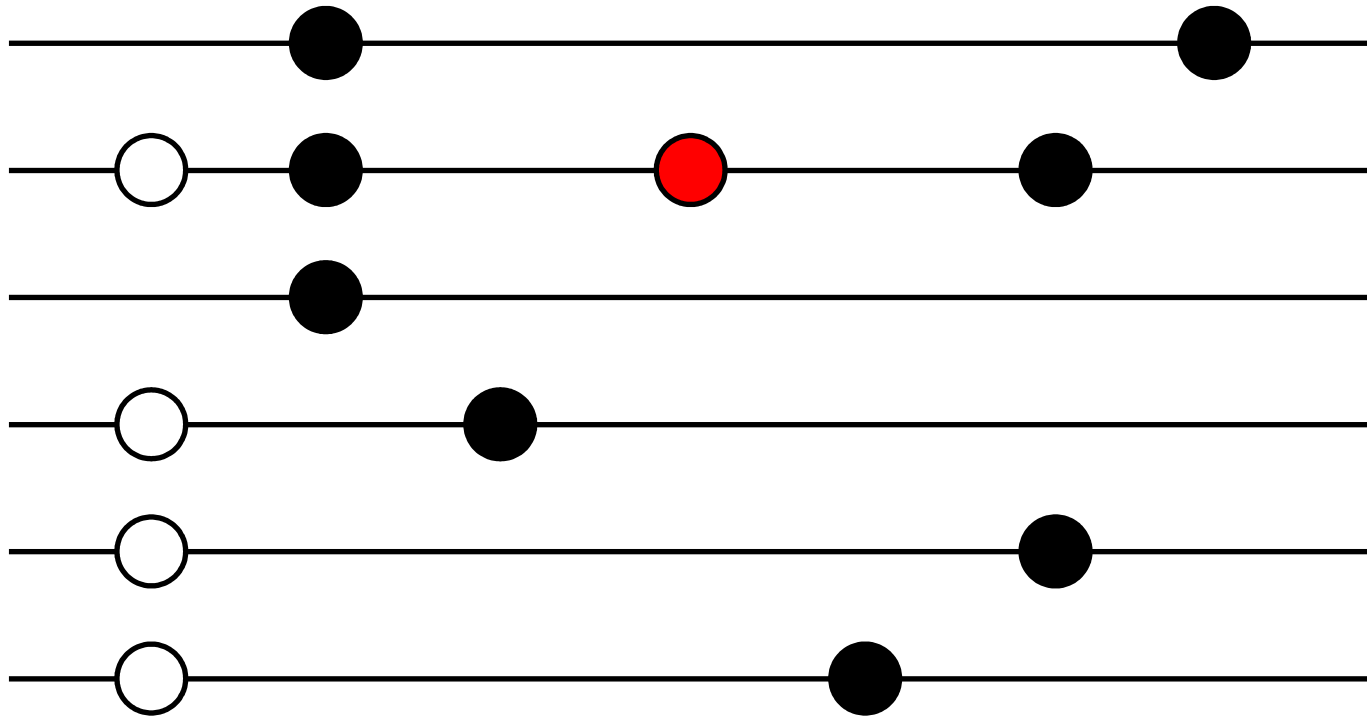
1974: Maynard-Smith and Haigh

The hitch-hiking effect of a favourable gene.

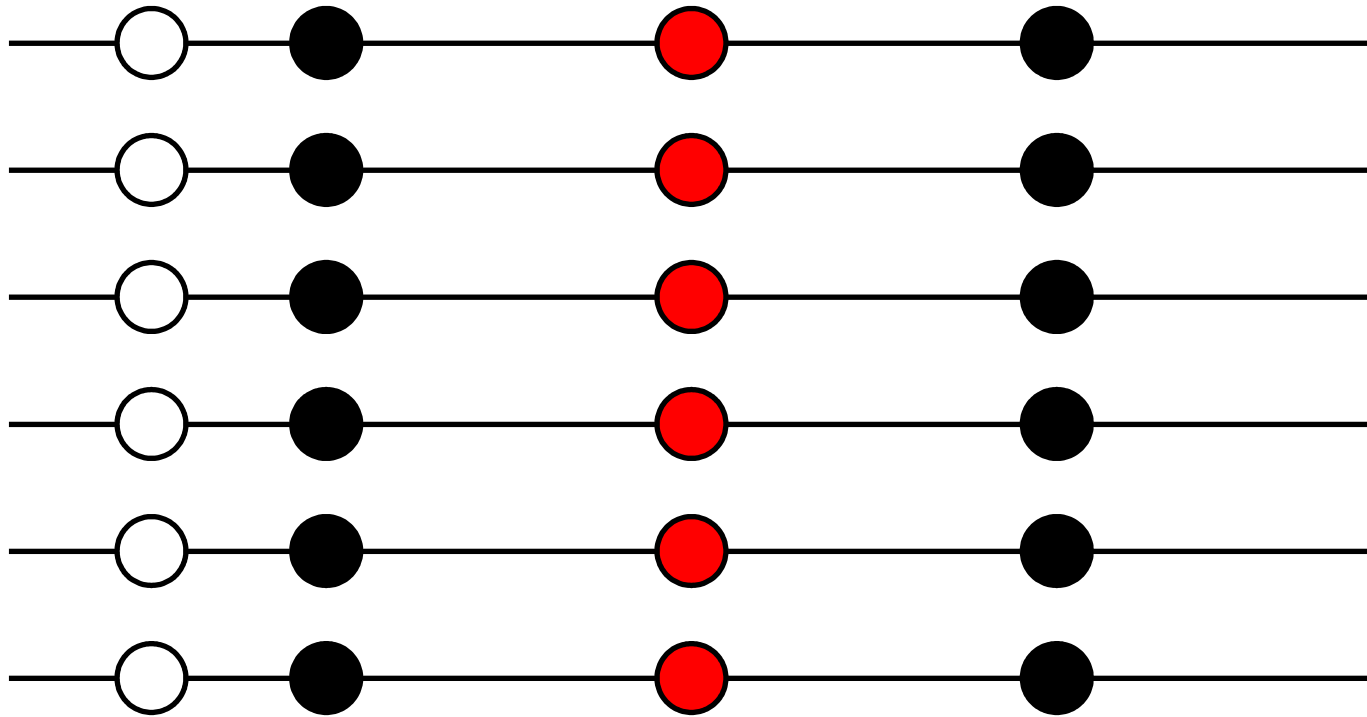
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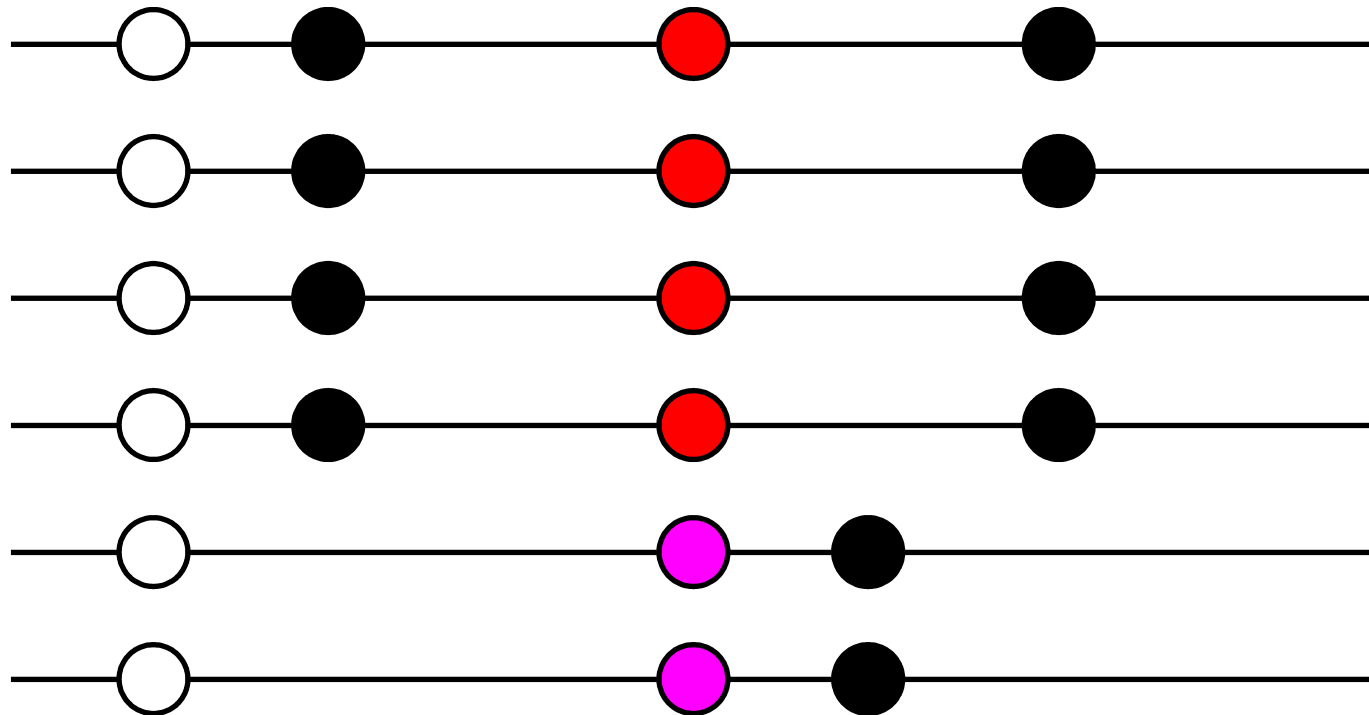
# Classical (hard) sweep



# Classical (hard) sweep



# Adaptation may not leave a sweep signature



# Sweeps have lost some of their appeal



although some human adaptive evolution may have occurred via classic selective sweeps, this is likely to be the exception rather than the rule



## HUMAN EVOLUTION

# Sweep model is swept away

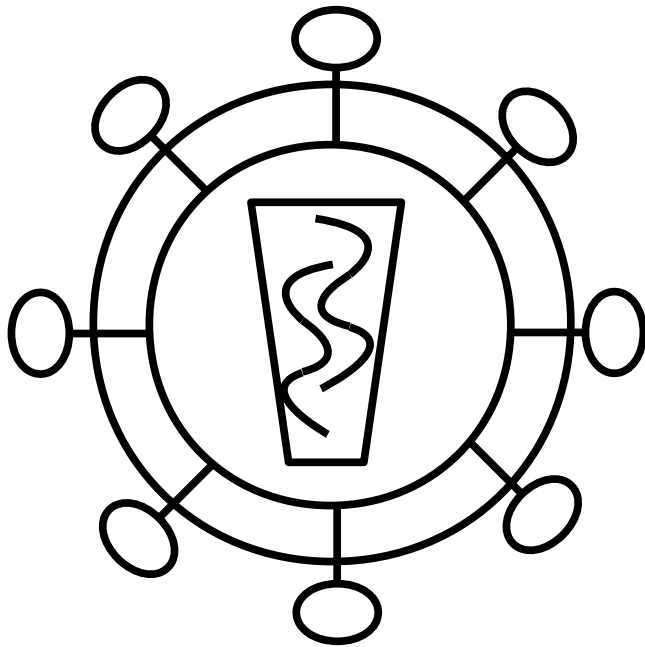
Efforts to identify the genetic basis of human-specific adaptations have mainly looked for evidence of classic selective sweeps, which happen when a new, advantageous mutation is rapidly fixed in a population. However, a new study suggests that classic selective sweeps have been rare in

genomes generated by the 1000 Genomes Project — a more direct approach that also overcomes the ascertainment bias of genotyping. Consistent with selective sweeps, they found reduced levels of diversity around exons and conserved non-coding regions — the areas that

populations, or at least extreme differences in allele frequencies between the populations. However, when the authors looked at alleles that are highly differentiated between populations, they found little evidence of enrichment for alleles that cause amino-acid changes or affect a

# Why study sweeps in HIV?

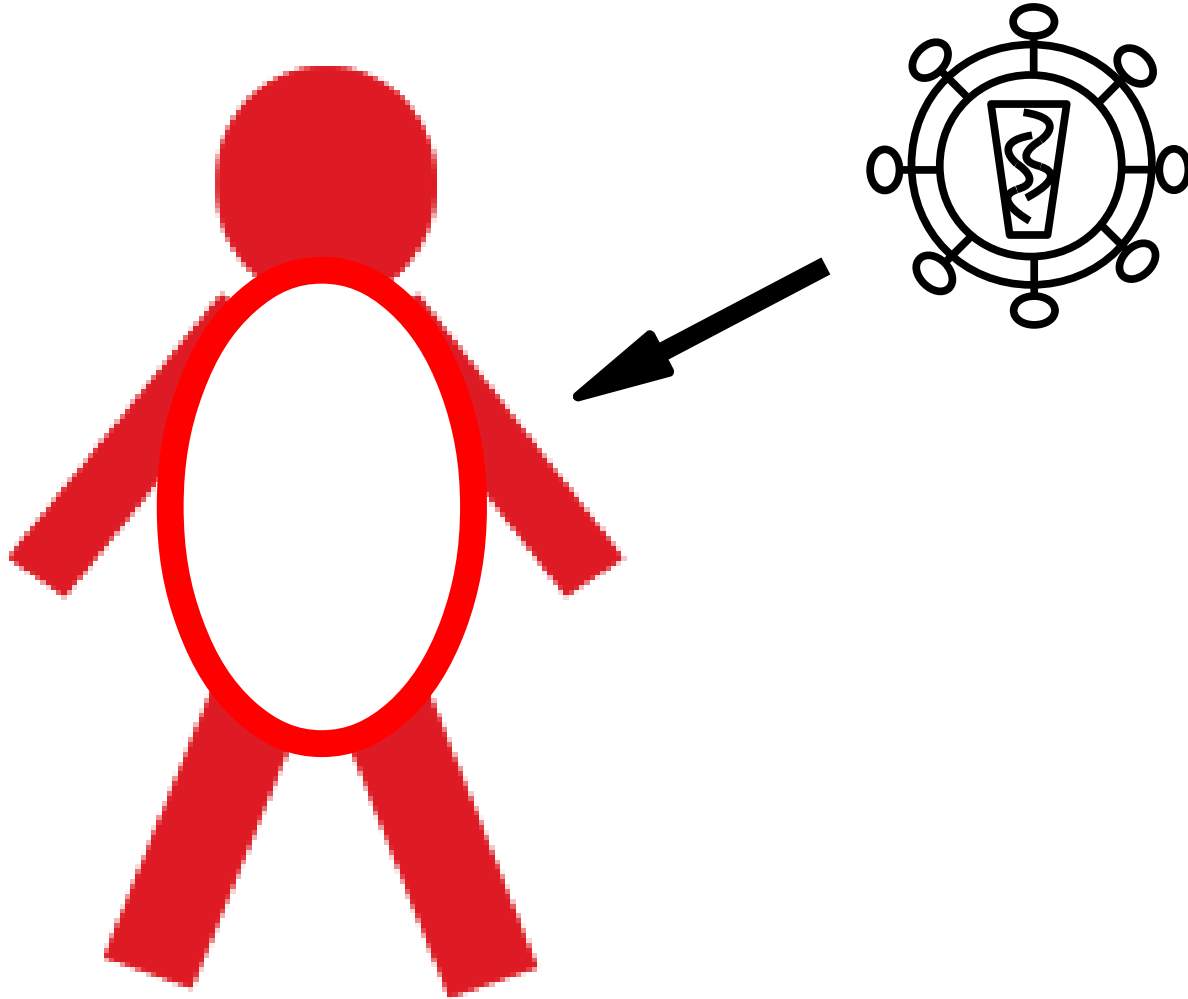
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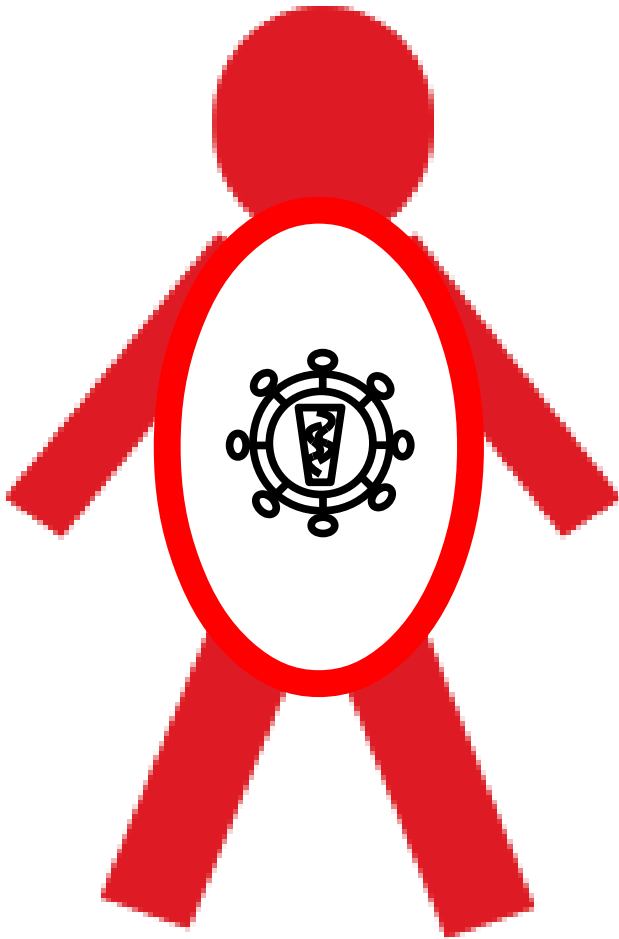
# A patient is infected once

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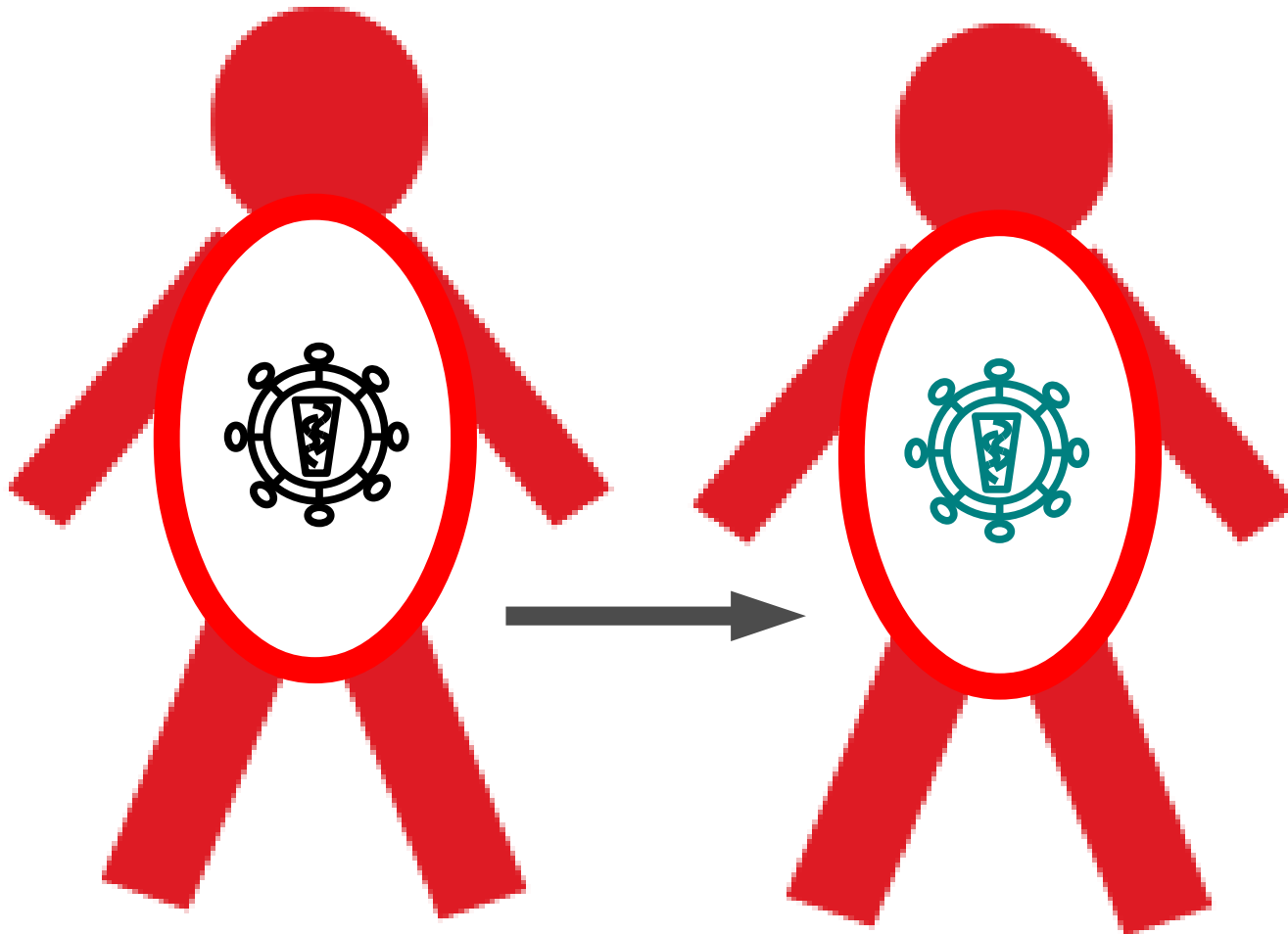
# Virus is stuck in the patient

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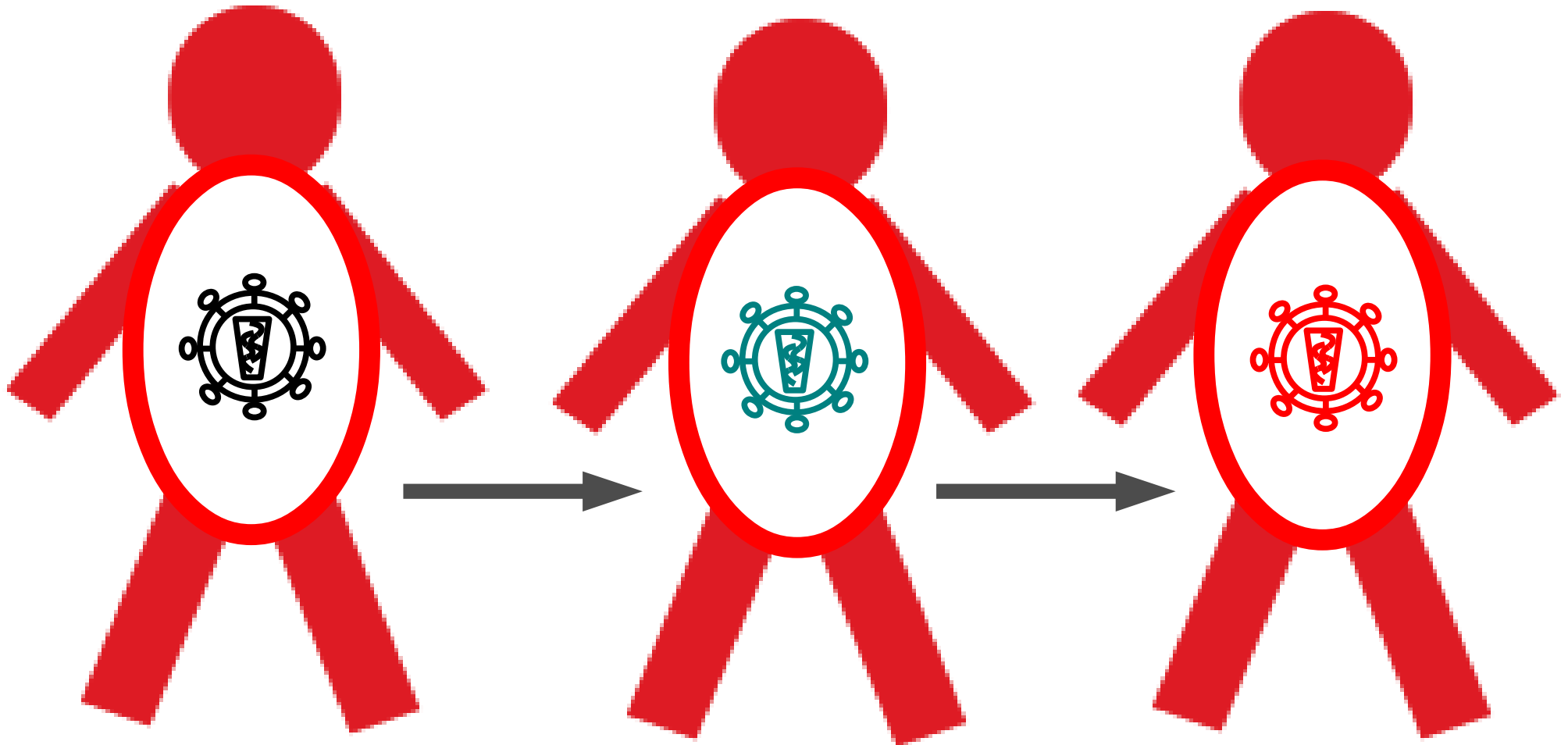


# Follow patient / virus over time

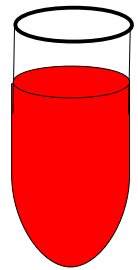
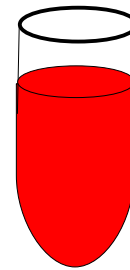
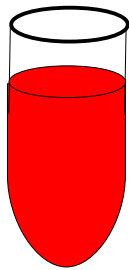
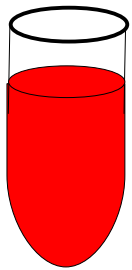
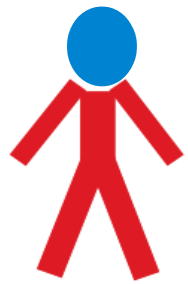
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# Follow patient / virus over time



# Follow patient / virus over time



# Beneficial mutations known

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TCCCTAGT**A**TAGTCTCT

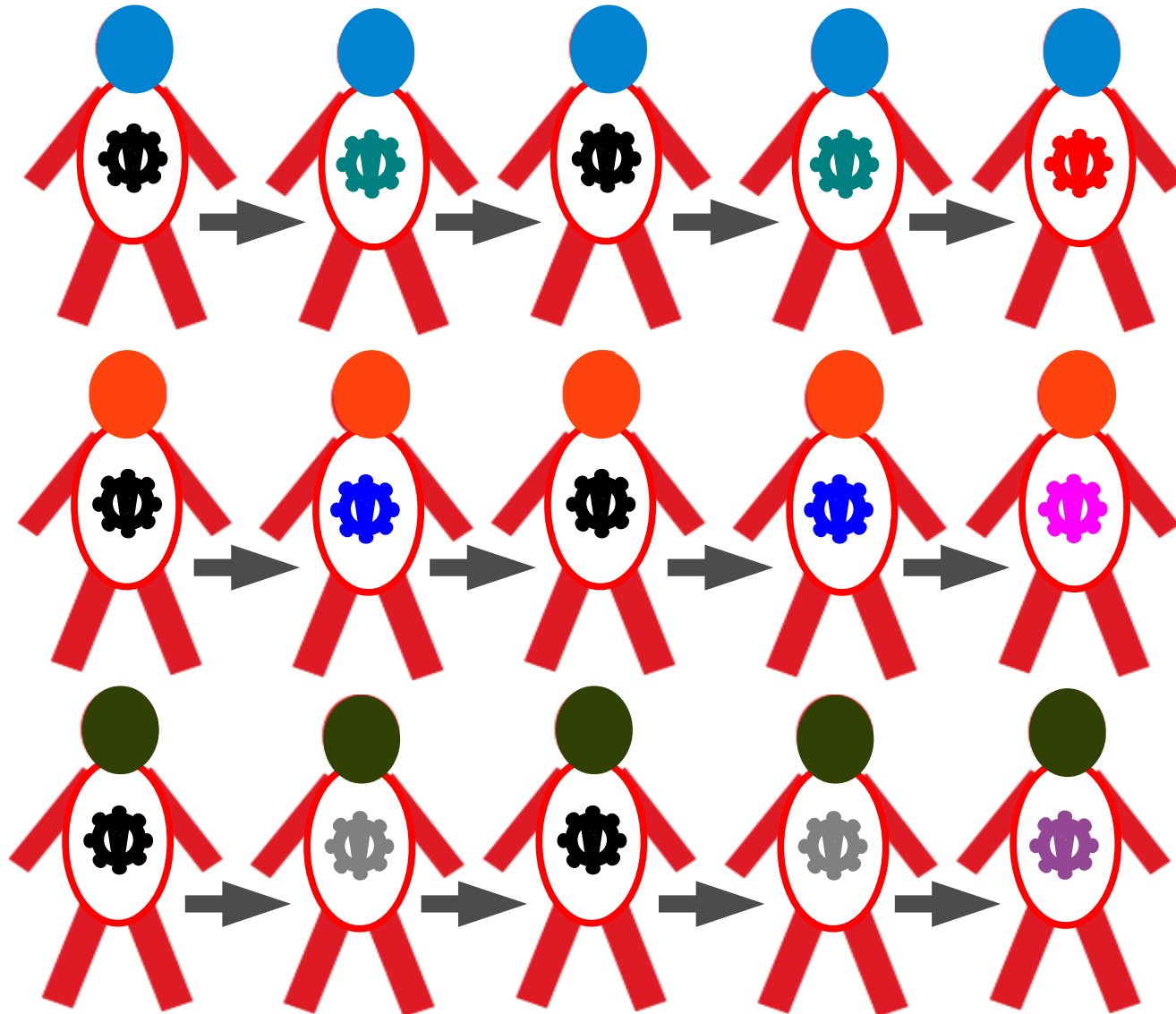
not resistant



TCCCTAGT**T**TAGTCTCT

resistant

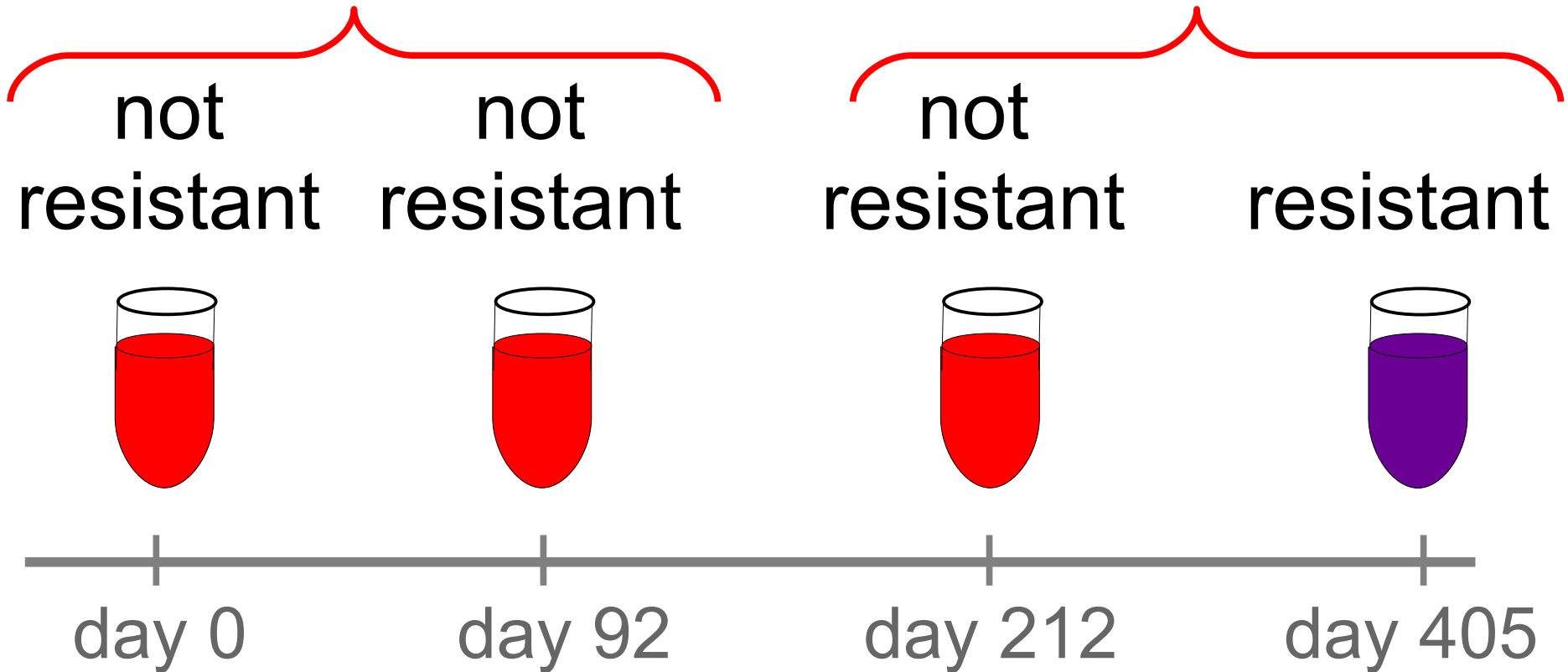
# We can follow many patients



# Data for current study

27 x control

30 x fixation

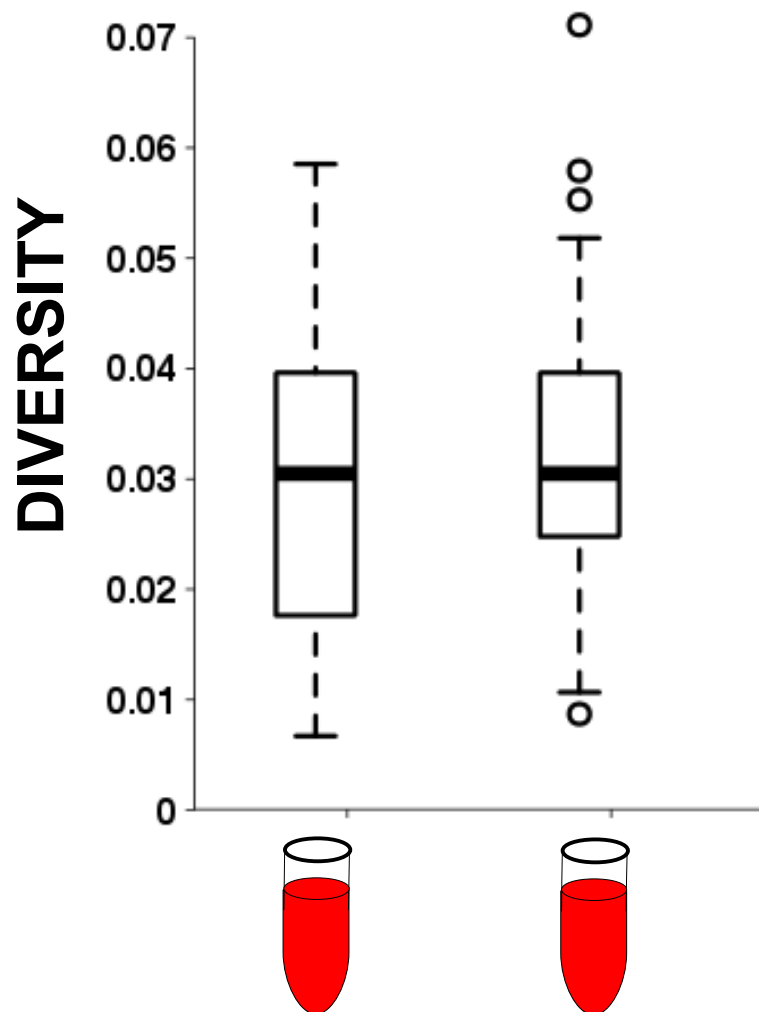


(Data from Bacheler et al, 2000, AAC)

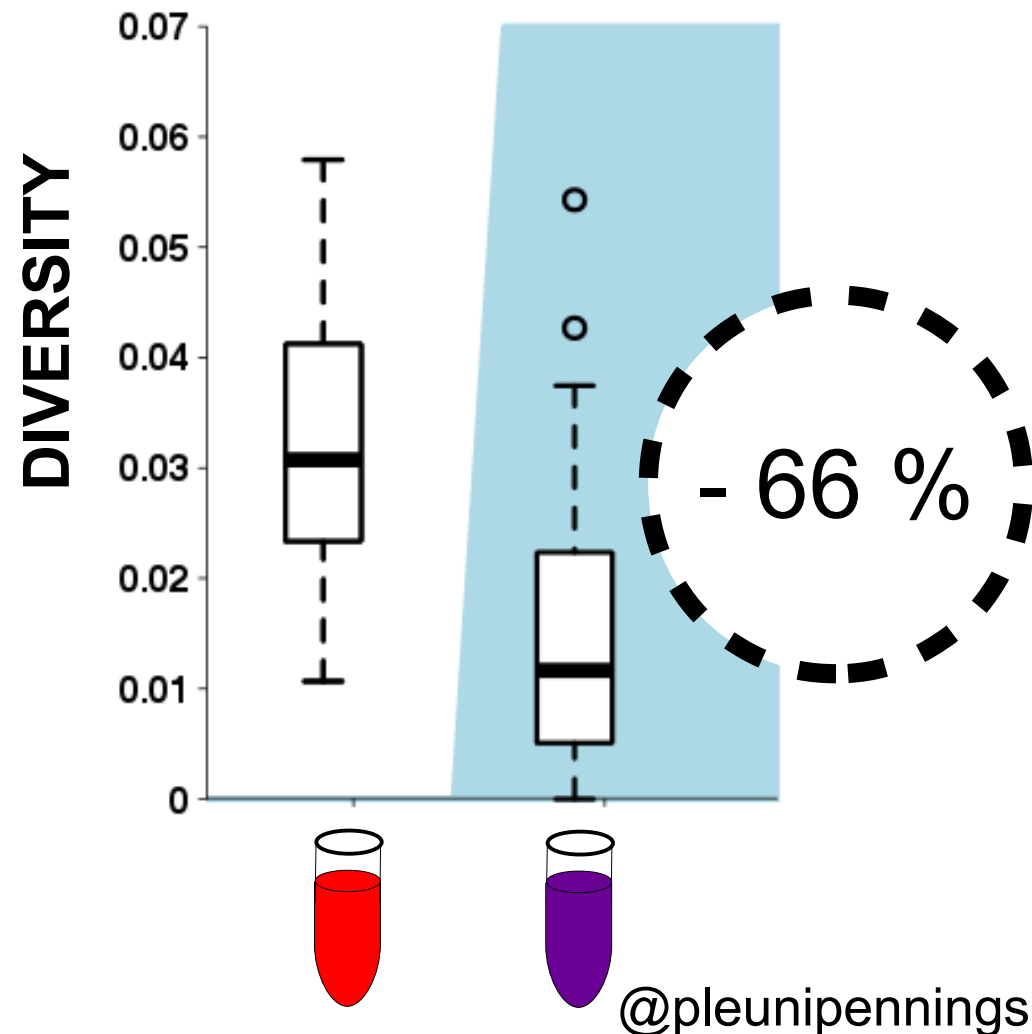


# Fixation of resistance mutation reduces diversity

27 x control



30 x fixation



# Both hard and soft sweeps occur

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30 x fixation



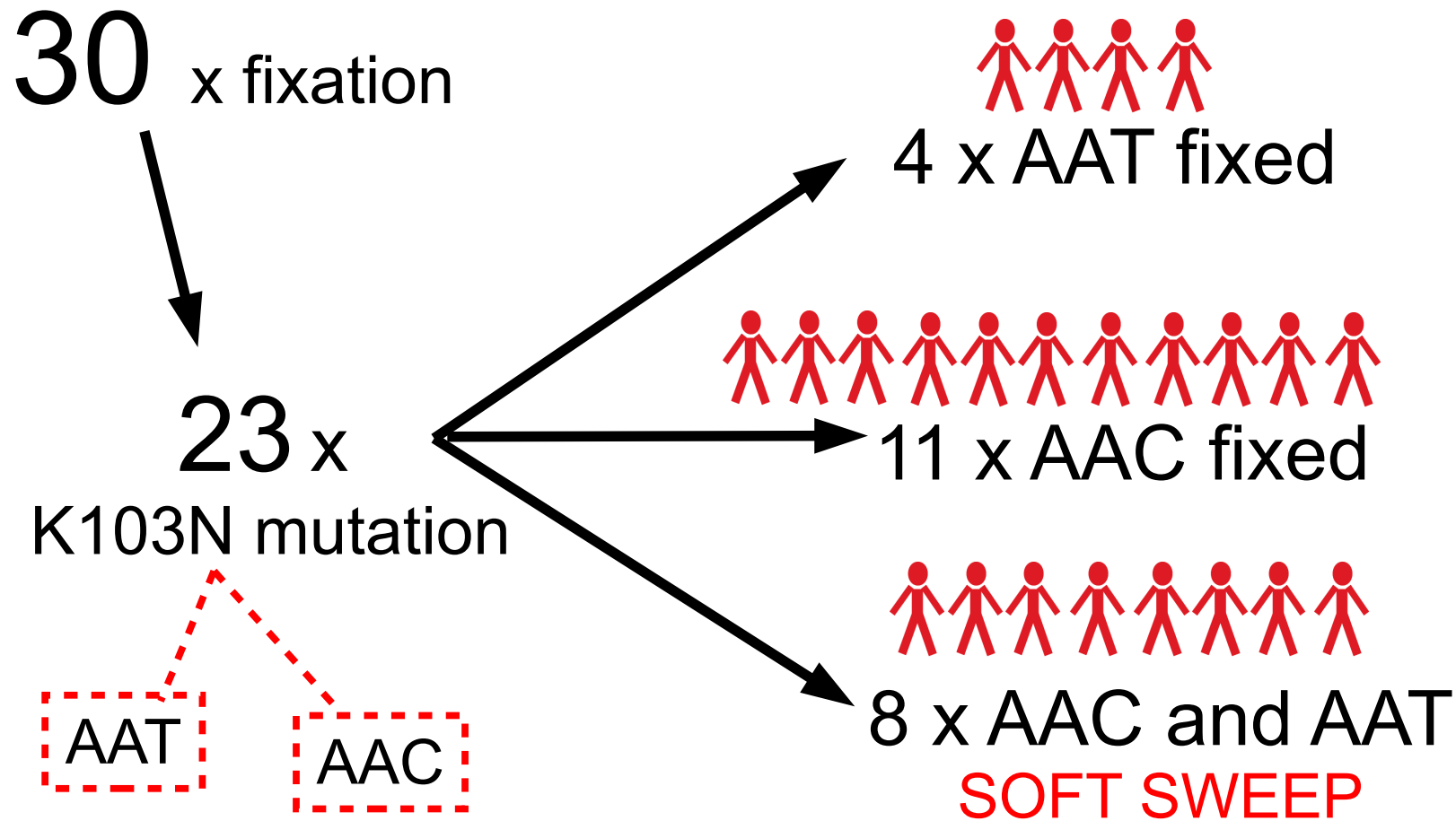
23 x

K103N mutation

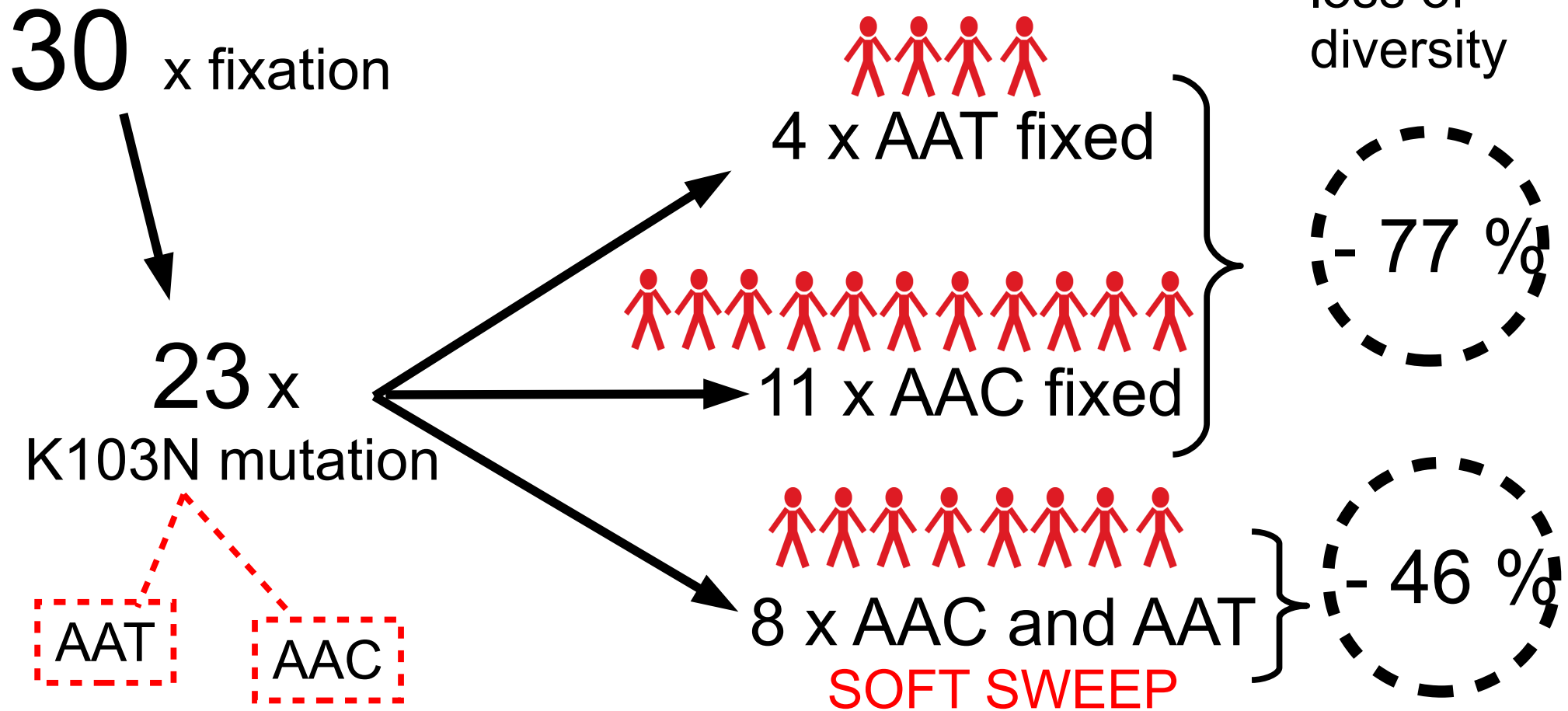
AAT

AAC

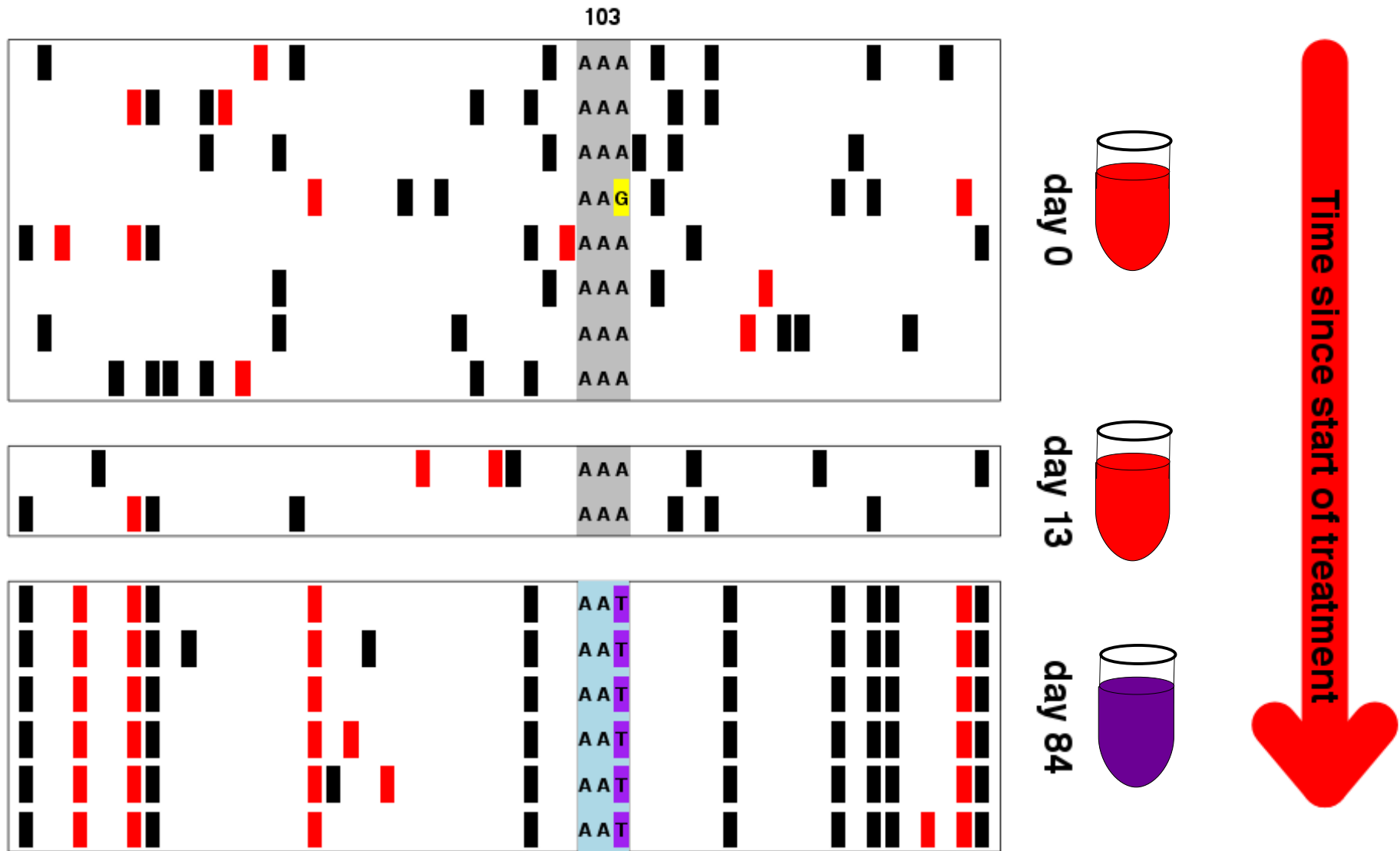
# Both hard and soft sweeps occur



# Both hard and soft sweeps occur

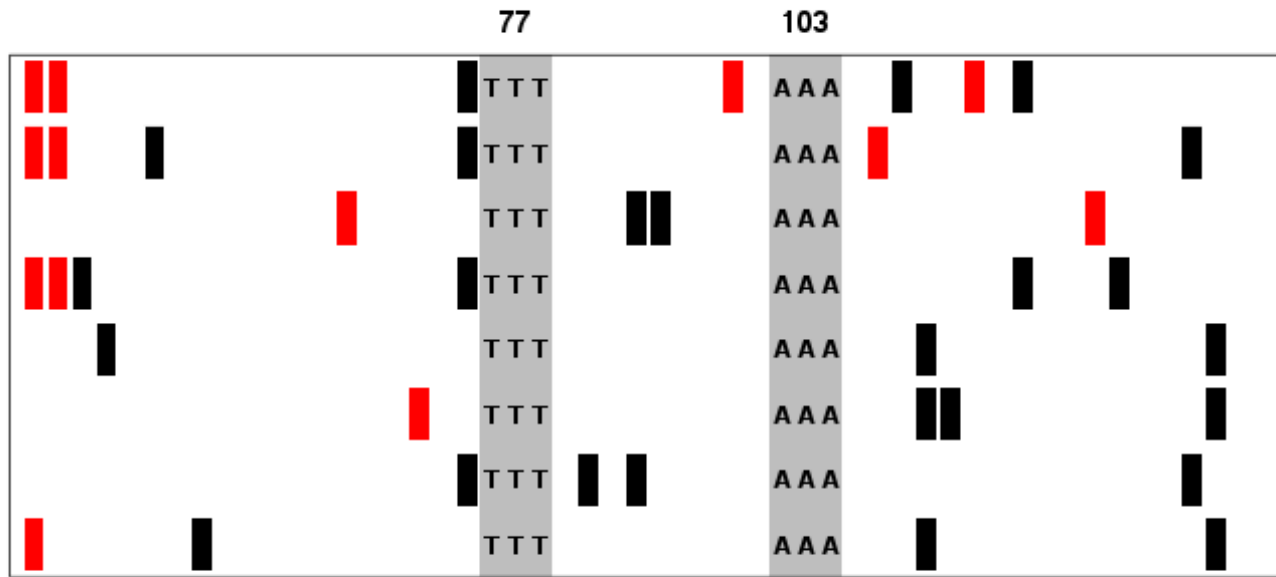


# Hard sweep example

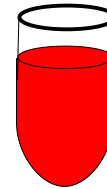


REVERSE TRANSCRIPTASE

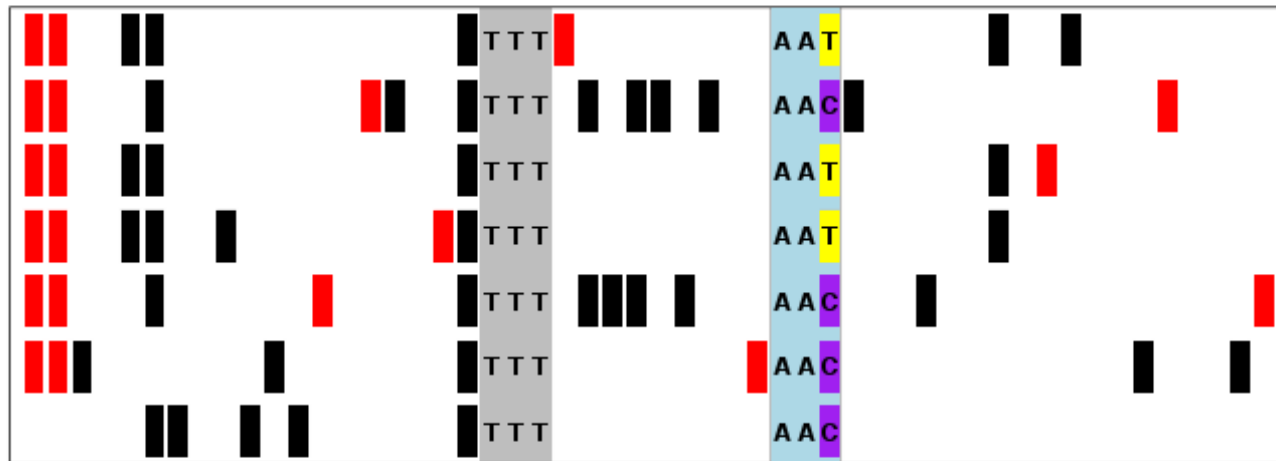
# Soft sweep example



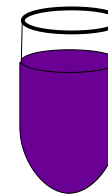
day 0



Time since start of treatment

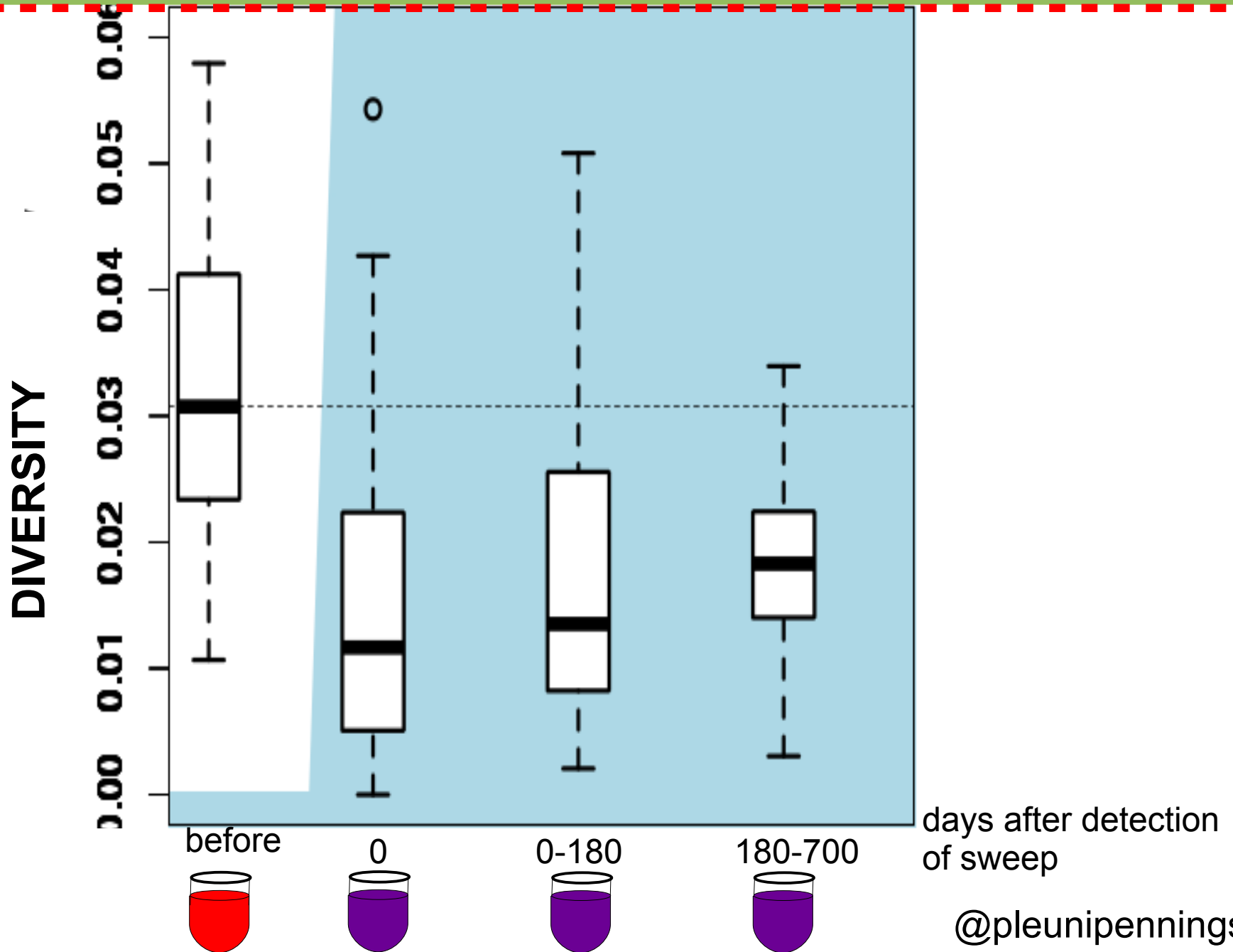


day 28



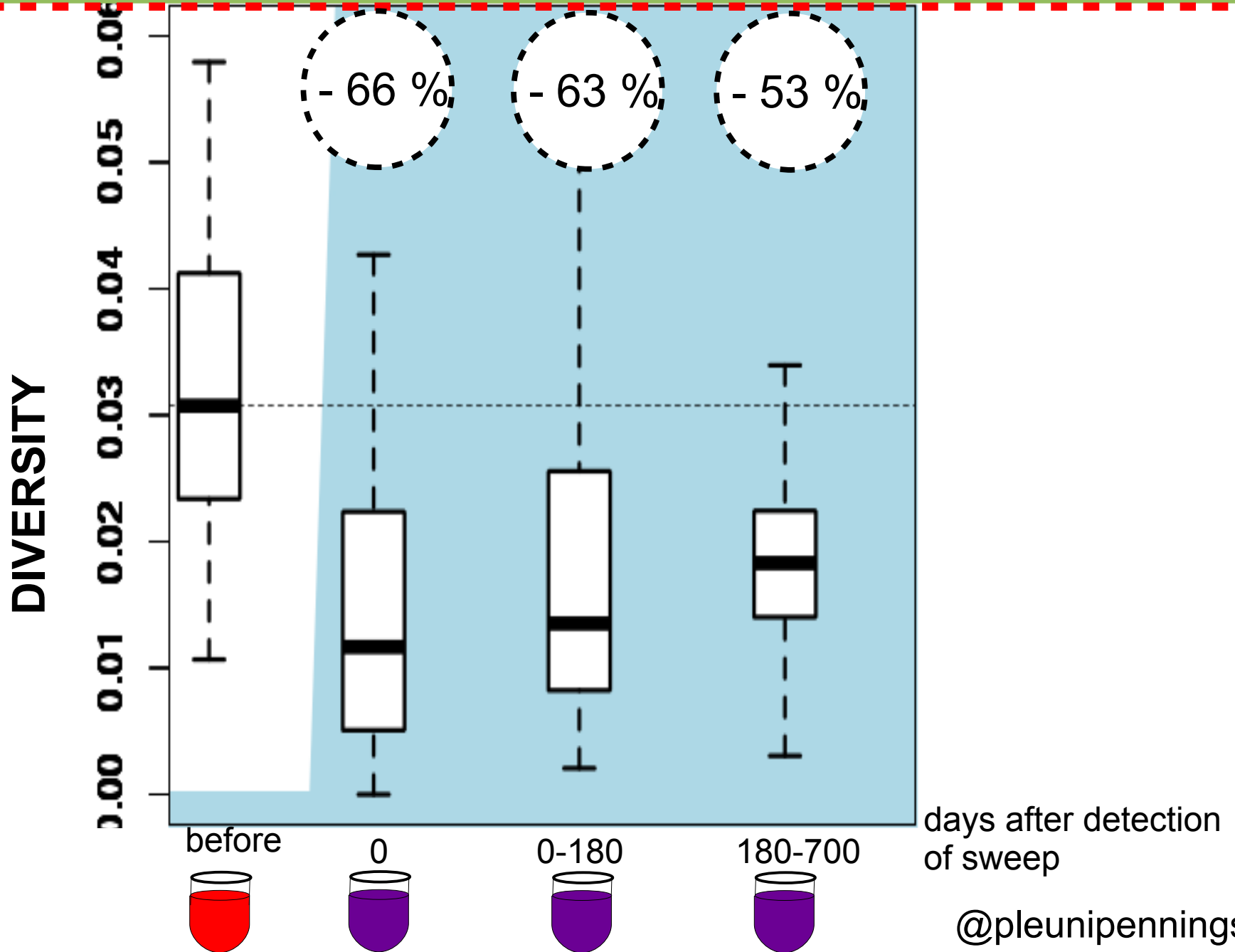
REVERSE TRANSCRIPTASE

# Diversity recovers



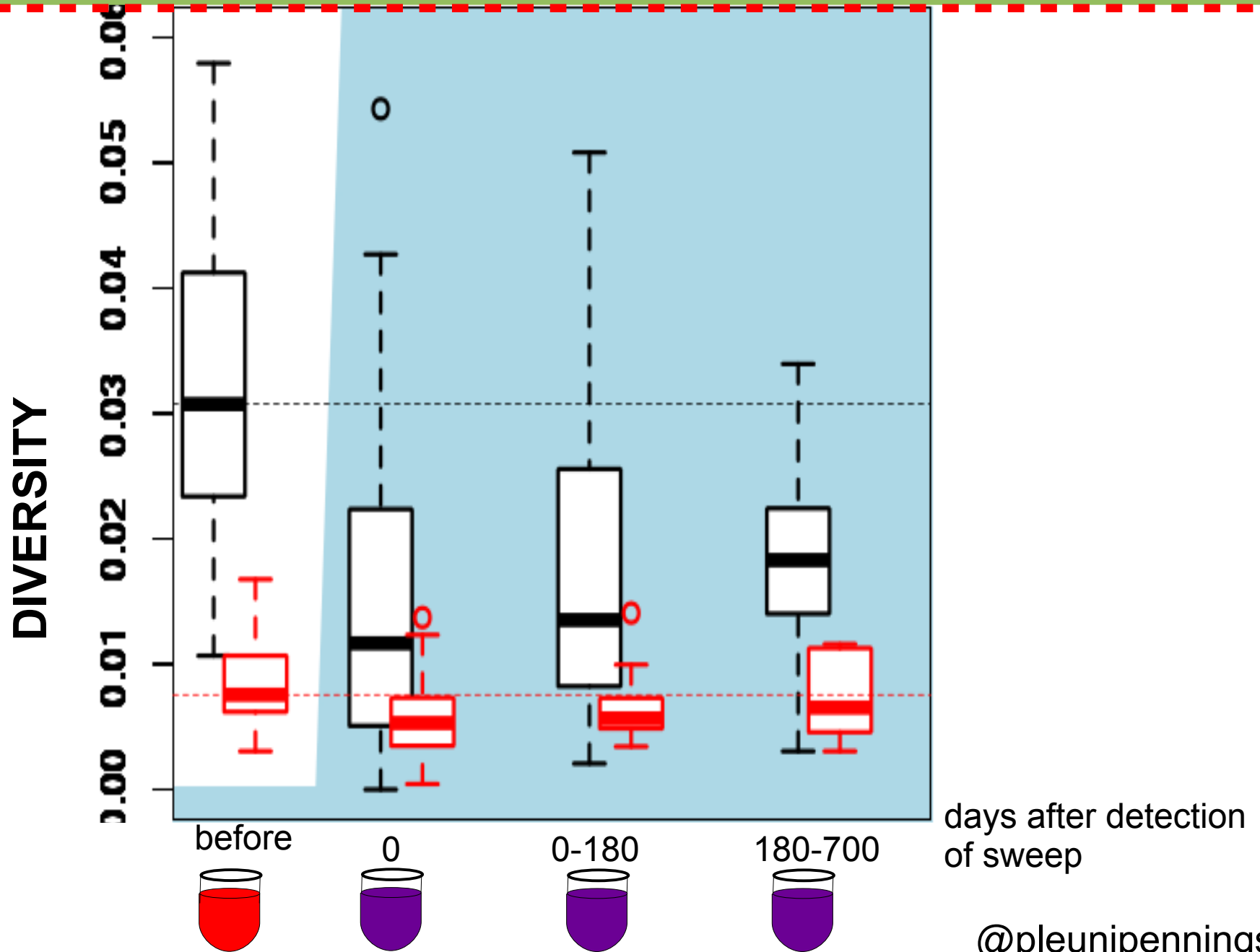
@pleunipennings

# Diversity recovers

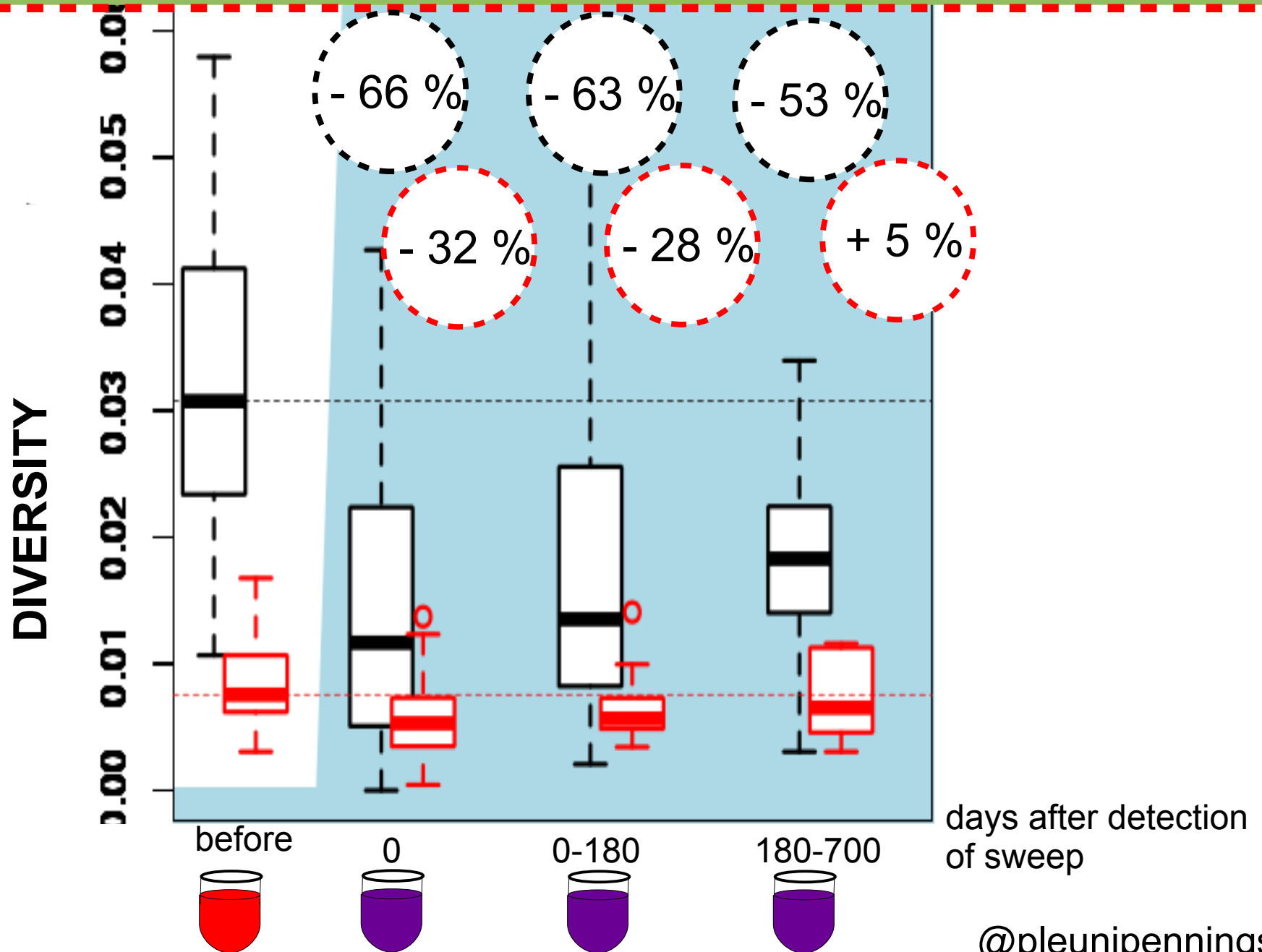




# Non-synonymous sites recover faster

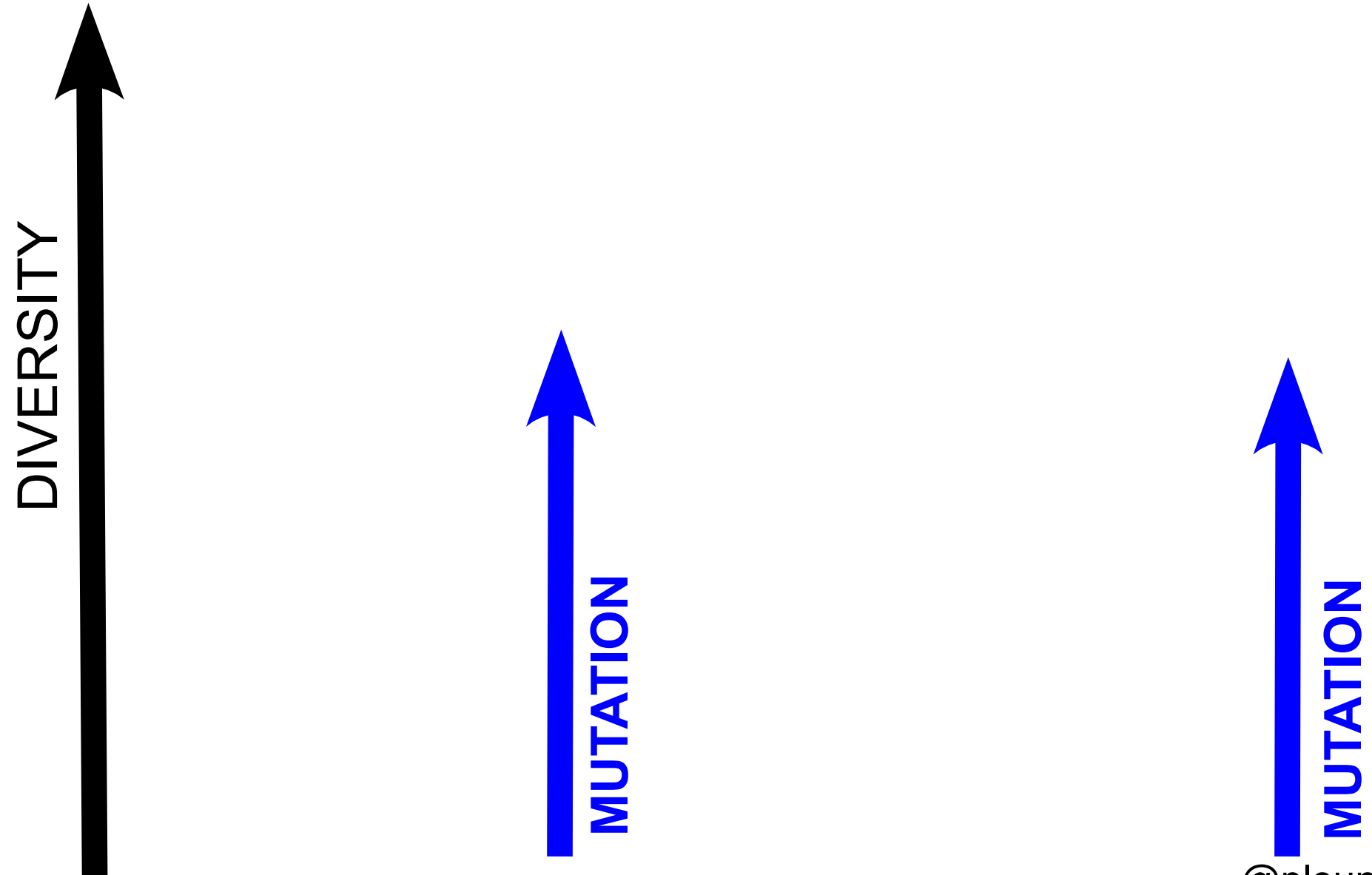


# Non-synonymous sites recover faster

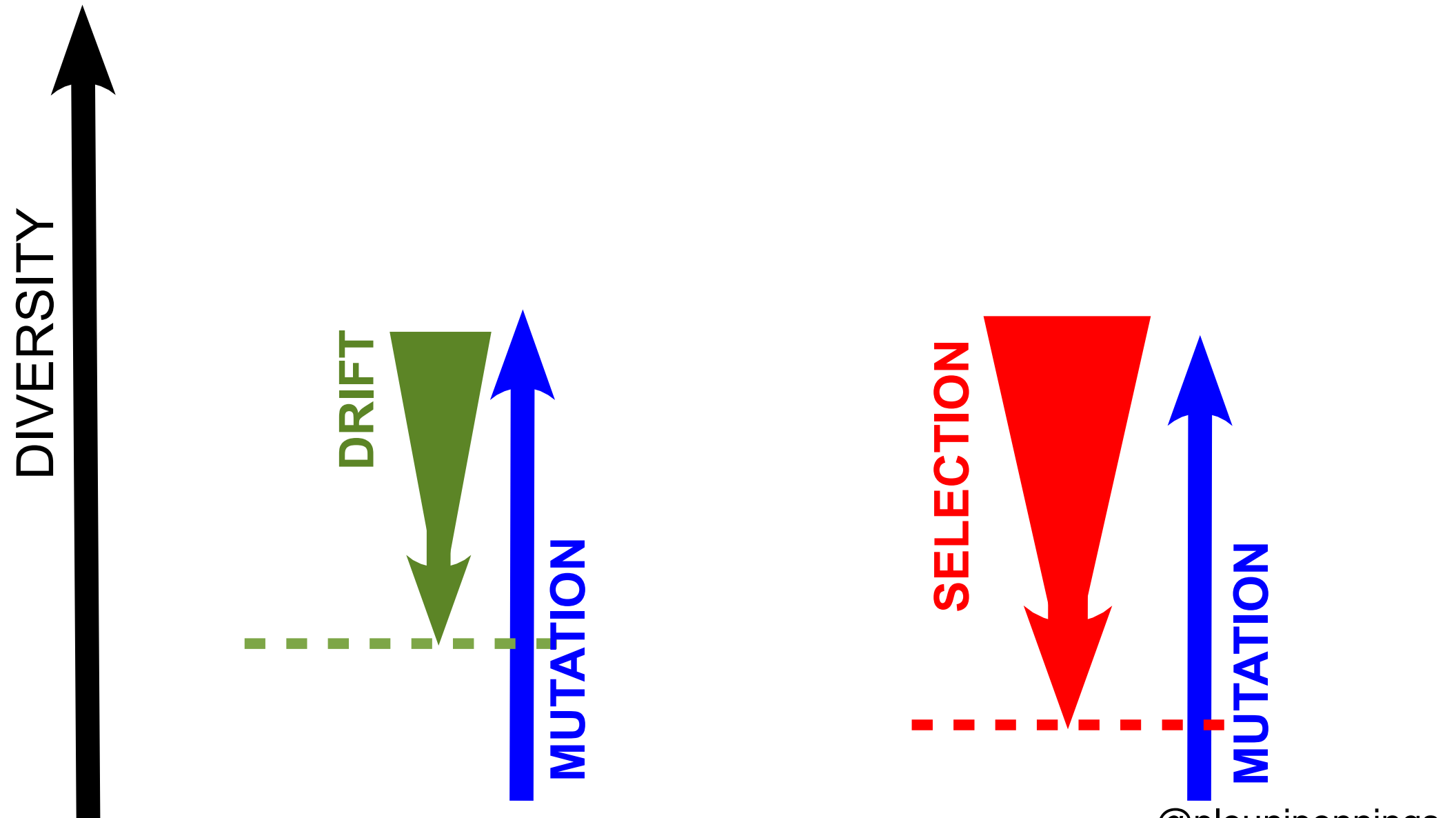


# Why is recovery faster for non-synonymous sites?

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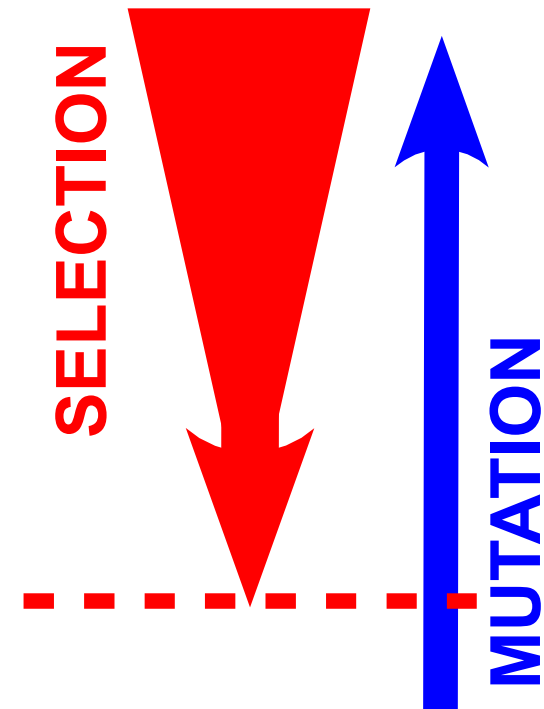
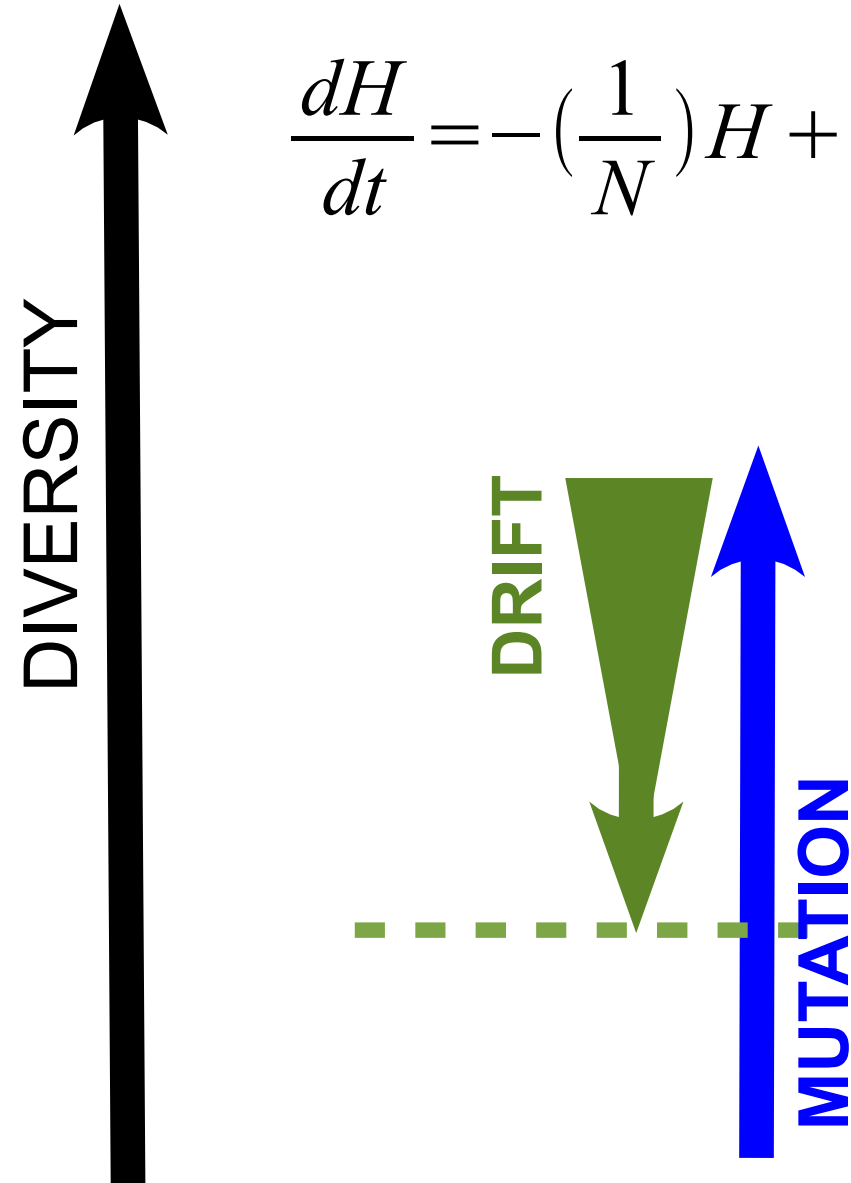
# Negative feedback speeds recovery



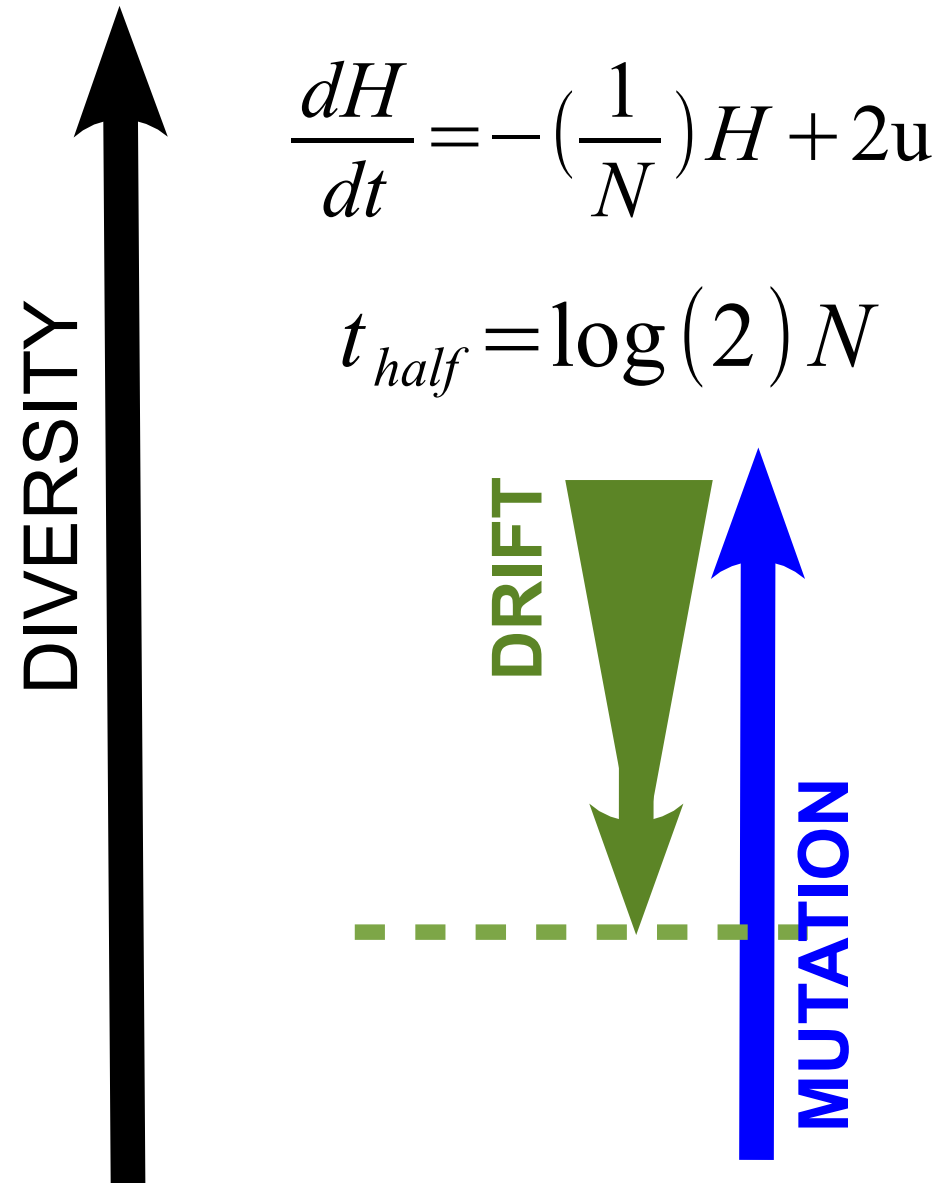
# Negative feedback speeds recovery

$$\frac{dH}{dt} = -\left(\frac{1}{N}\right)H + 2u$$

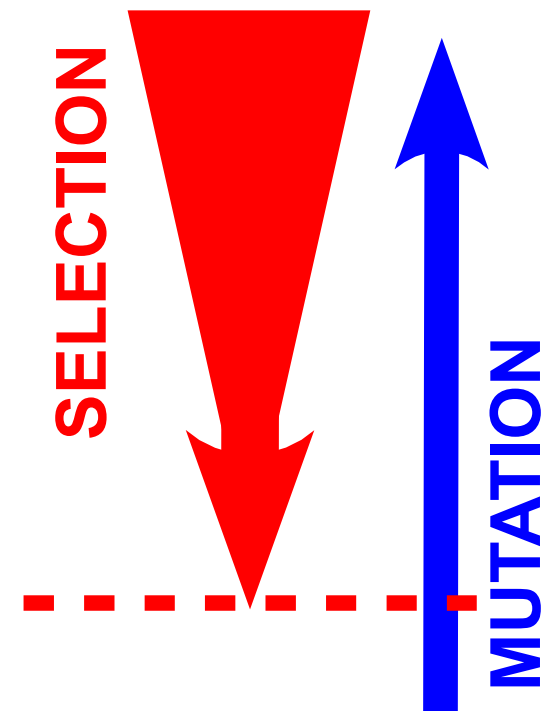
$$\frac{dH}{dt} = -sH + 2u$$



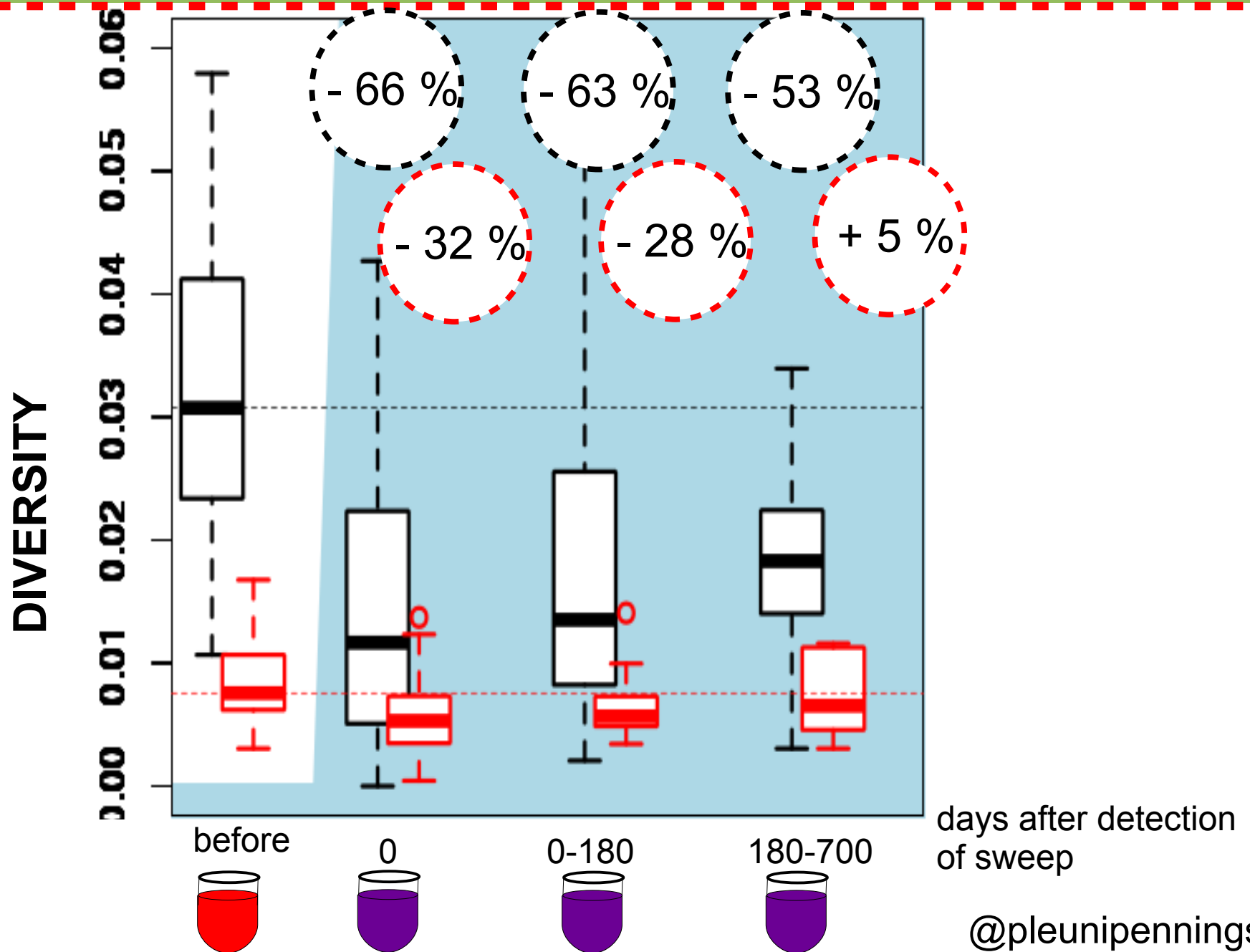
# Negative feedback speeds recovery



$$\frac{dH}{dt} = -sH + 2u$$
$$t_{half} = \log(2) / s$$



# Non-synonymous sites recover faster



# Non-synonymous sites recover faster

THANK YOU!

