R_o

- The average number of offspring per capita that survive to reproductive age, reproductive output
- In ID, the average number of infections produced by an infected individual in a susceptible population

  R_o< 1, self-sustaining epidemic is not possible

  R_o~ 1, early stochastic events may extinguish invader, but epidemic is possible, typical of endemic disease

  Large R_o, Epidemic is virtually certain

- In some diseases R is not a homogeneous value (remember Ro may differ from R)
- Differs from R_e (R_t)

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Main source of susceptible hosts

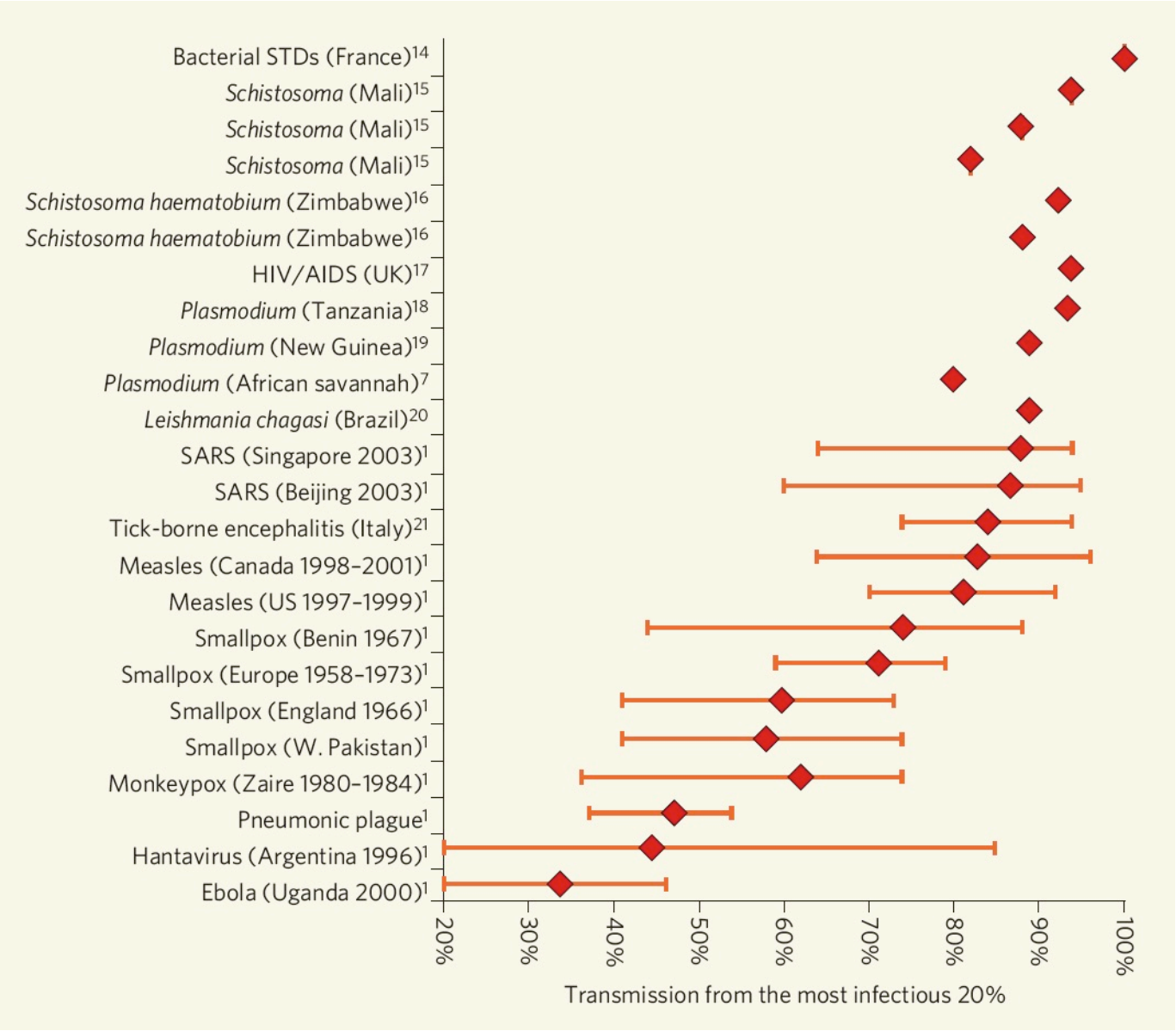
- Newborns (*post maternal protection*)
- Decay of immune memory
- Evolution of antigenicity
- Migration

Ro not a homogenous value throughout the population?

Superspreaders

- Individuals are not homogeneous in infectiousness
- Superspreading occurs in all diseases (albeit a greater or lesser extent depending on the disease)
- Heterogeneities in patterns of sexual partner acquisition (gonorrhea, HIV) primarily based on contact differences among individuals
- Differences in parasite burdens with helminth infections
- Heterogeneous biting by malaria vectors
- Control efforts should focus on these individuals
- Events are also being classified as “superspreader events” in the COVID-19 pandemic

Heterogeneity in infectiousness for a range of diseases



•The 20/XX index, 20% of the most infectious individuals are responsible for XX% of the transmission

Galvani & May, 2005

Today, there are ~ 1,400 currently recognized *species* of **human** pathogens

500- bacterial

300- fungi

300- helminths

200- viruses

50- protozoa

2- prions

+ Variants

Microbes

Eukaryotes vs. Prokaryotes

Woolhouse, M.J., 2006

Do you think that this represents an abundant number of microbes?


Pathogen +/-
Commensal +/0
Mutualist +/+

Epidemiology terms (CDC)

Epidemiology- the branch of medicine that deals with the incidence, distribution and possible control of diseases and other factors relating to health.

Epidemic-the occurrence of more cases of *a specific* disease than expected in a given area or among a specific group of people over a particular period of time.

Outbreak- synonymous with epidemic. Alternatively, a localized as opposed to generalized epidemic.

Endemic-the constant presence of a disease or infectious agent within a given geographic area or population group; may also refer to the usual prevalence of a given disease within such area or group.

Pandemic=WHO alert status phase 6; an epidemic occurring over a very wide area (several countries or continents) and usually affecting a large proportion of the population.


GREAT MARLBOROUGH STREET
PORTLAND STREET
WORK HOUSE
BROAD STREET
PULTENEY STREET
GOLDEN SQUARE
PUMP

Three factors needed for a pandemic to occur

1. A new species/variant must emerge (no pre-existing immunity in most of the host population)
2. Must be pathogenic
3. Must be easily transmissible (via droplets, handshakes etc.)

Ok let's move onto……

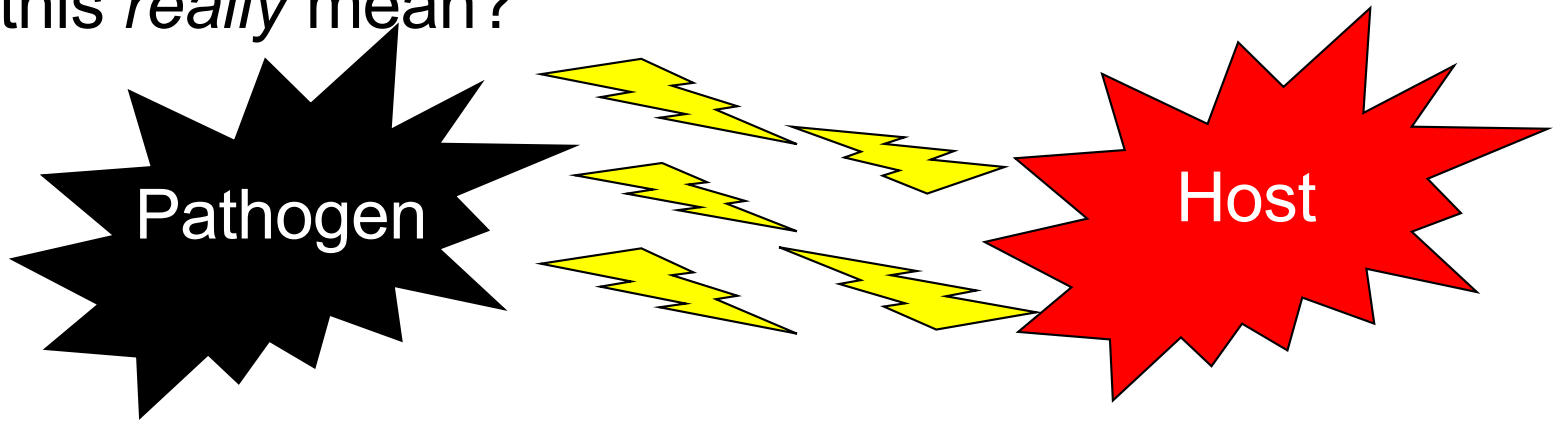
1. Why do pathogen's evolve so fast?
2. What are some of the basic traits that pathogens can evolve?
3. What is virulence, and how does it evolve?

Evolution- ‘Change of life through time’

Why do pathogens evolve so quickly?

The constant arms race between pathogen and host

Pathogens constantly change their genetic makeup to evade host defenses (and vice versa)….what does this *really* mean?



Provides a great example of Red Queen Hypothesis (antagonistic coevolution) !

Evolution- ‘Change of life through time’

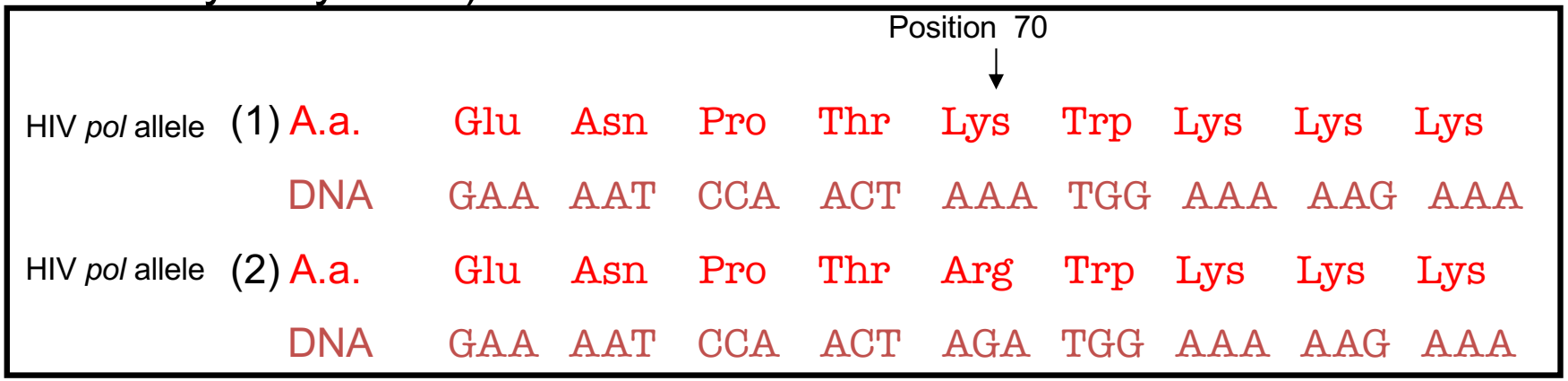
Pathogens evolve QUICKLY due to;

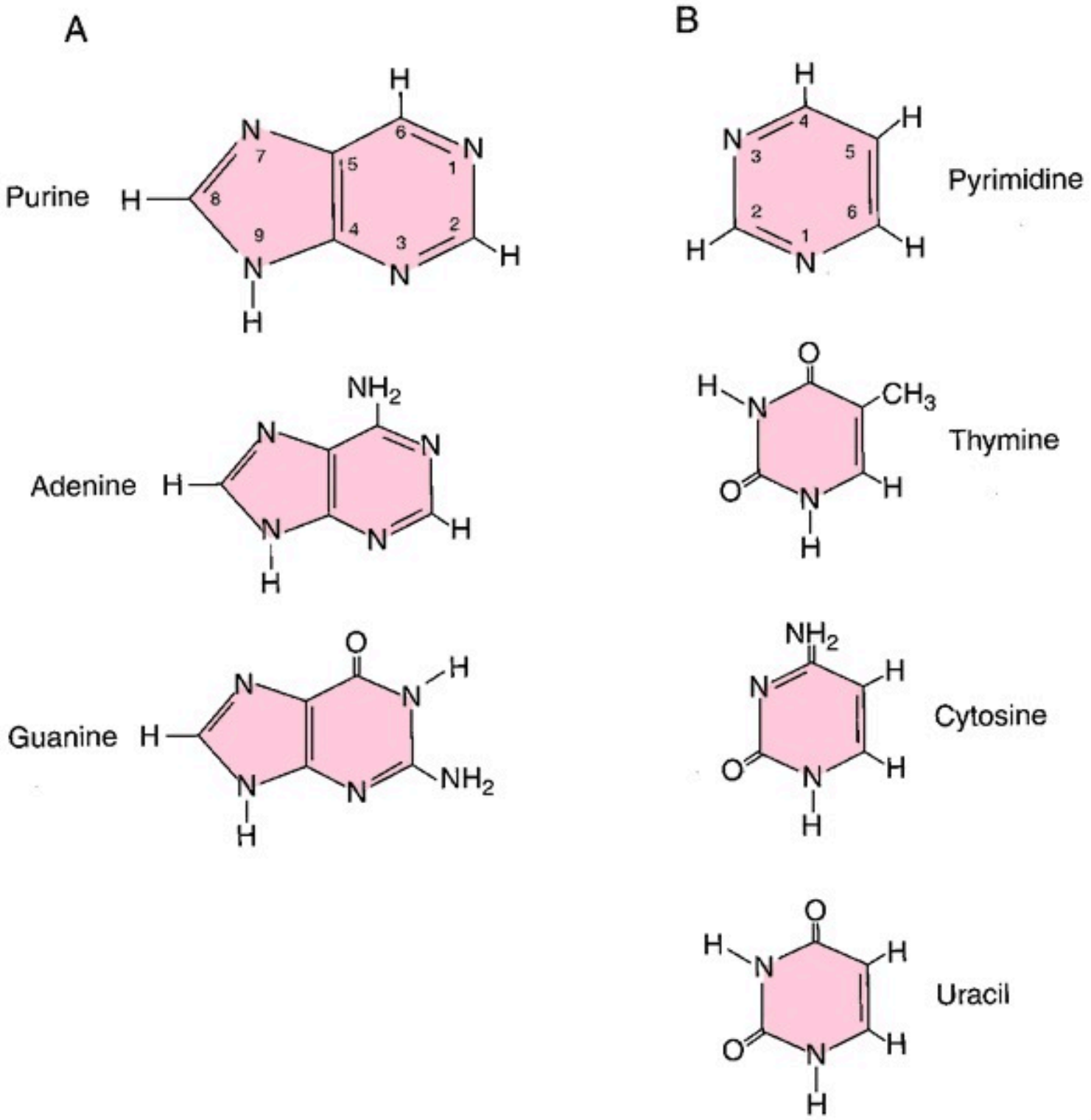
1. High population sizes
2. Short generation times
3. High mutation rates

Why is understanding pathogen evolution important, relative to medicine?

Mutations-the raw material of evolutionary change

- Changes in running order of bases, give rise to alleles
- Transitions, transversions, indels
- Rates vary tremendously among species (10^{-9} to 10^{-2} mutations/base/yr)
- Caused by faulty replication, spontaneous, exposure to mutagens
- May or may not be inherited
- May or may not affect the protein level (synonymous vs nonsynonymous)




A
B
Purine
Adenine
Guanine
Pyrimidine
Thymine
Cytosine
Uracil

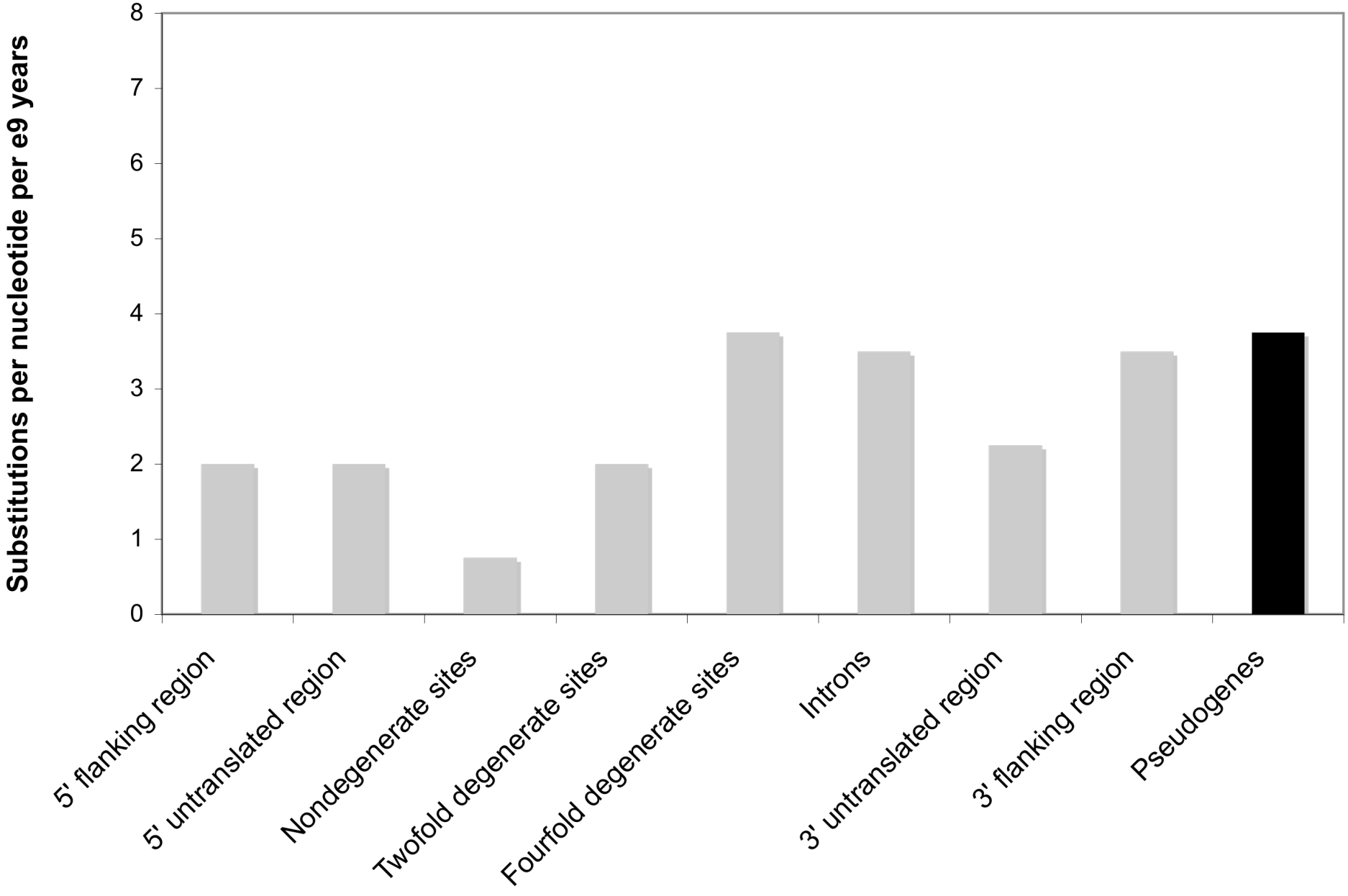
Genetic code

- Each amino acid (a.a.) specified by 3 consecutive, nonoverlapping nt (codons)
- 64 possible codons
- Degenerate
- 1 START codon
- 3 STOP codon (do not encode any a.a.)

First base in codon	Second base in codon: U	C	A	G	Third base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

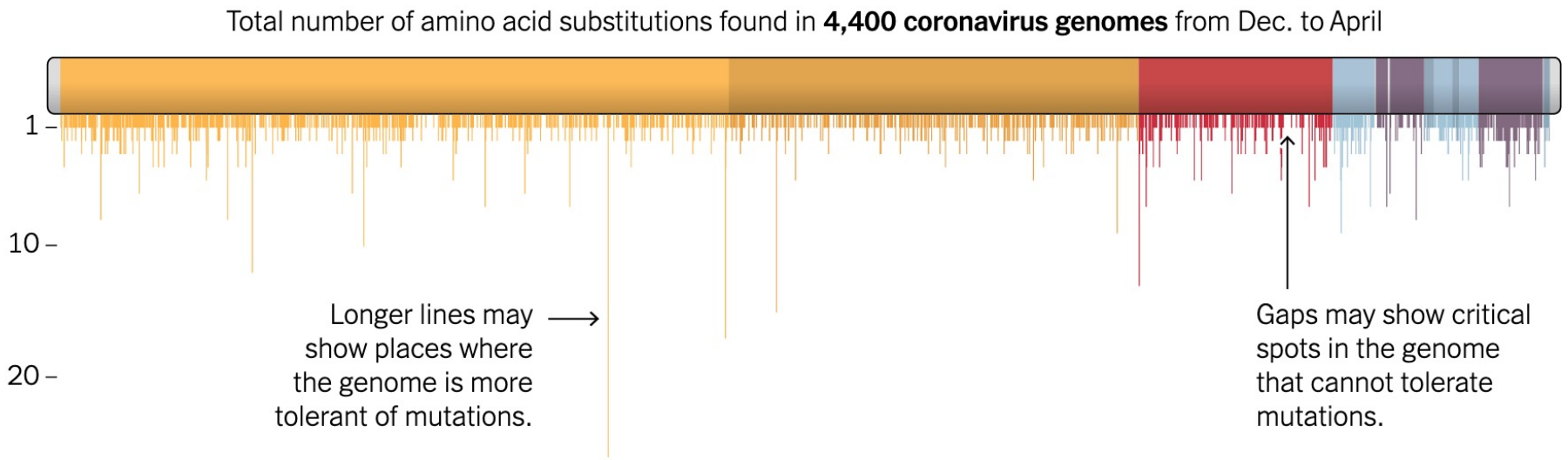
http://www.clcbio.com/scienceimages/genetic_code.png

Different regions of DNA sequence have varying probabilities of mutation



Li & Grauer, 1991

Mutations along the SARS-CoV-2 genome



- Nonsynonymous mutations have stronger natural selection constraints than synonymous mutations, why?
- Do mutations stick around? Purifying versus Diversifying selection.

Do mutations stick around? Depends at the phenotypic level…

Bad-decrease in fitness (high fitness cost) - removed through selection.

Good- increase in fitness (low fitness cost)- retained through selection.

Neutral- (no fitness cost) free from natural selection. These can be fixed through genetic drift.

Genetic drift

- Changes in the frequency of a genetic variant in the population owing to chance alone
- Greater effects in smaller populations

Why?

Modes of selection at the sequence level

Negative (purifying) selection= $d_N < d_S$

Positive (diversifying) selection= $d_N > d_S$

Mutations

- The great majority of sequences show negative or neutral selection.
- Pathogen **antigens** often show +ve selection, as they change to escape host immunity. Some of the best examples of +ve selection involves the evolution of resistance to antibiotics, drugs, and pesticides.
- Other pathogen protein domains low d_N (-ve selection) due to functional or structural constraints and hidden from external recognition.
- Can be used to understand transmission chains

- Why do pathogens differ in virulence (host harm), why the difference in Ebola vs. rhinovirus (common cold)?

- Why do pathogens differ in virulence (host harm), why the difference in Ebola vs. rhinovirus (common cold)?

”Transmission and virulence, the yin and yang” of infectious diseases and pathogen ecology”

Quammen, 2013