Viral genetics

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VIRAL GENETICS

- VIRUSES GROW RAPIDLY
- A SINGLE PARTICLE PRODUCES A LOT OF PROGENY
- DNA VIRUSES SEEM TO HAVE ACCESS TO PROOF READING, RNA VIRUSES DO NOT SEEM TO

NATURE OF GENOMES

- RNA or DNA
- SEGMENTED OR NON-SEGMENTED

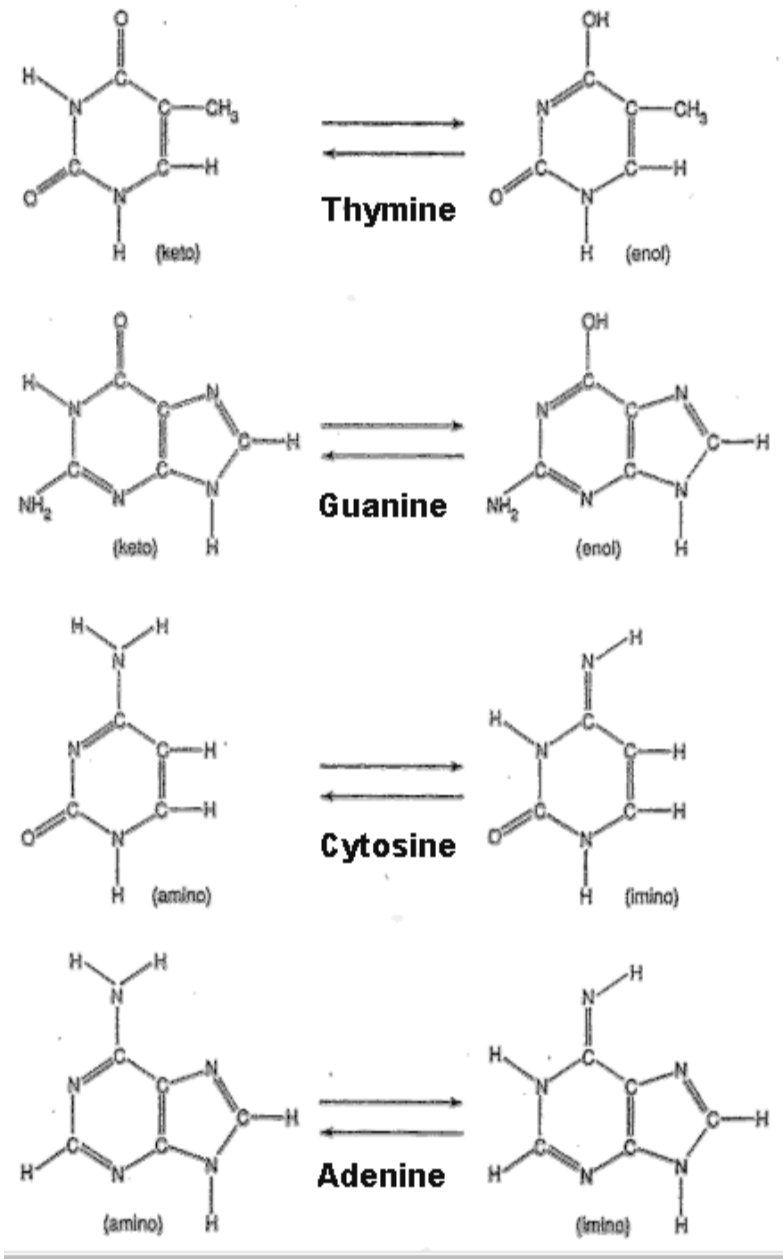
GENETIC CHANGE

- MUTATION 
- RECOMBINATION

ORIGIN OF MUTATIONS

- SPONTANEOUS
  - tautomeric form of bases
    - A base is changed by the repositioning of a hydrogen atom, altering the hydrogen bonding pattern of that base resulting in incorrect base pairing during replication
  - polymerase errors

Tautomeric forms of bases



most of time

rarely

ORIGIN OF MUTATIONS

- SPONTANEOUS
  - tautomeric form of bases
  - polymerase errors
  - mutation rates usually higher in RNA viruses (lack of proof reading)

- PHYSICALLY INDUCED
  - UV light , especially problem if no access to repair
  - X-rays
- CHEMICALLY INDUCED
  - Hydroxylamine NH_2OH
  - Alkylating agents

Types of mutations

- POINT: Caused by chemicals or malfunction of DNA replication, exchange a single nucleotide for another
  - Three types
    - Silent
    - Missense
    - Nonsense
- INSERTION
  - Frame shift
- DELETION
  - Alter the reading frame

PHENOTYPE

PHENOTYPE

- the observed properties of an organism

PHENOTYPIC CHANGES

- CONDITIONAL LETHAL - multiply under some conditions but not others - wild-type (wt) grows under both sets of conditions
- PLAQUE SIZE
  - may show altered pathogenicity
- DRUG RESISTANCE
  - important in the development of antiviral agents
- ENZYME-DEFICIENT MUTANTS
  - some genes can be ‘optional’ in certain circumstances
- ATTENUATED MUTANTS
  - milder (or no) symptoms
  - vaccine development

GENETIC CHANGE

- MUTATION
- RECOMBINATION

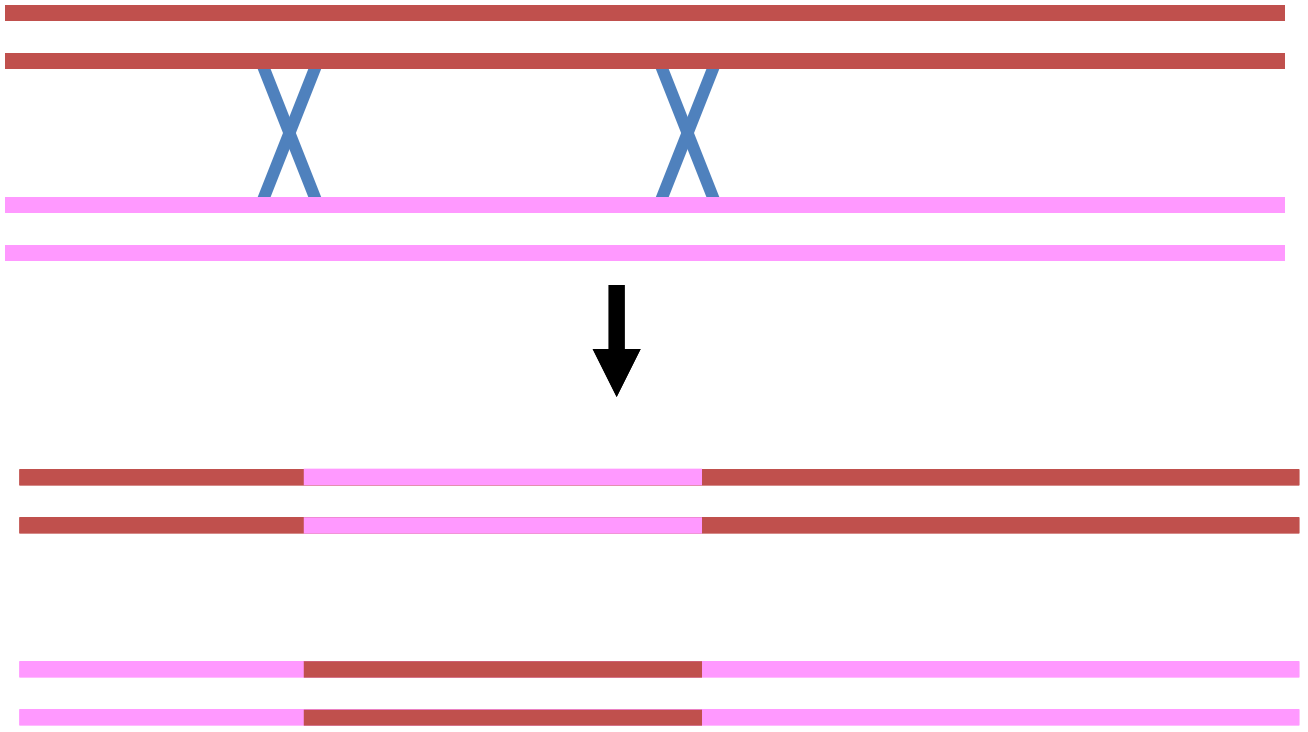
RECOMBINATION

Exchange of information between two genomes

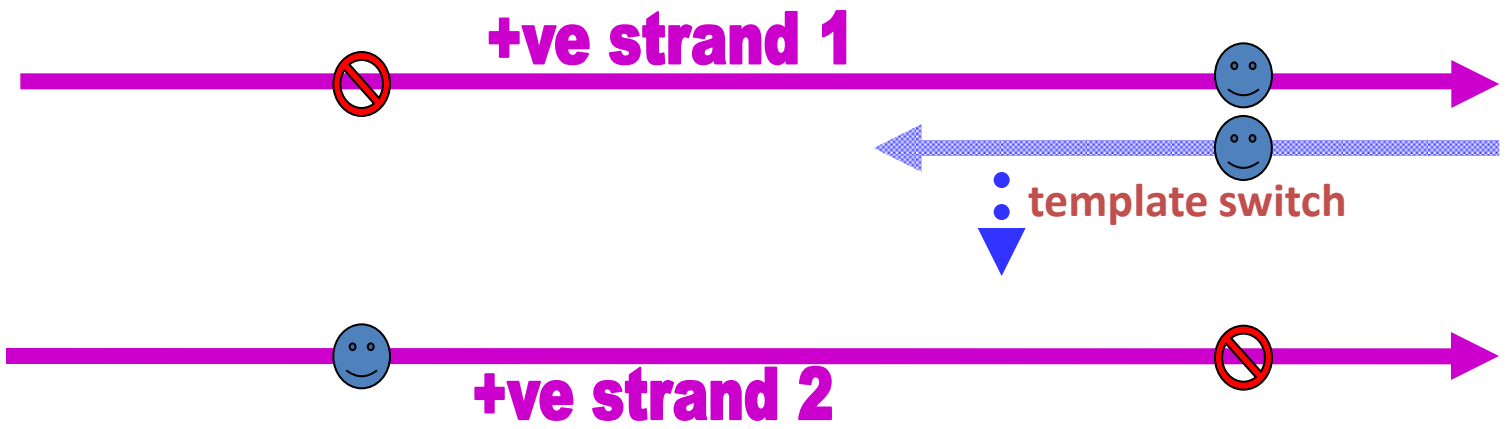
RECOMBINATION

‘classic’ recombination

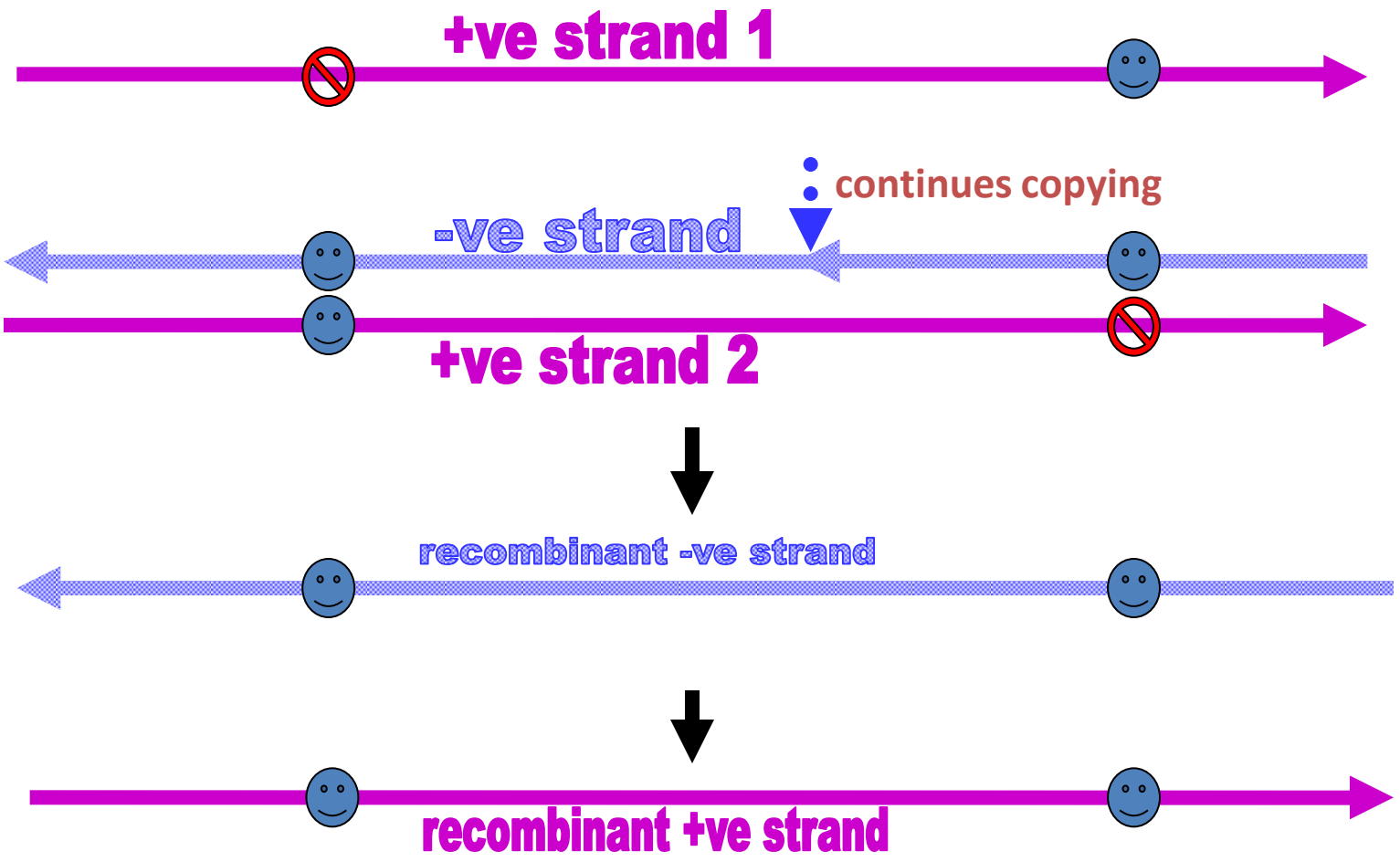
common in DNA viruses



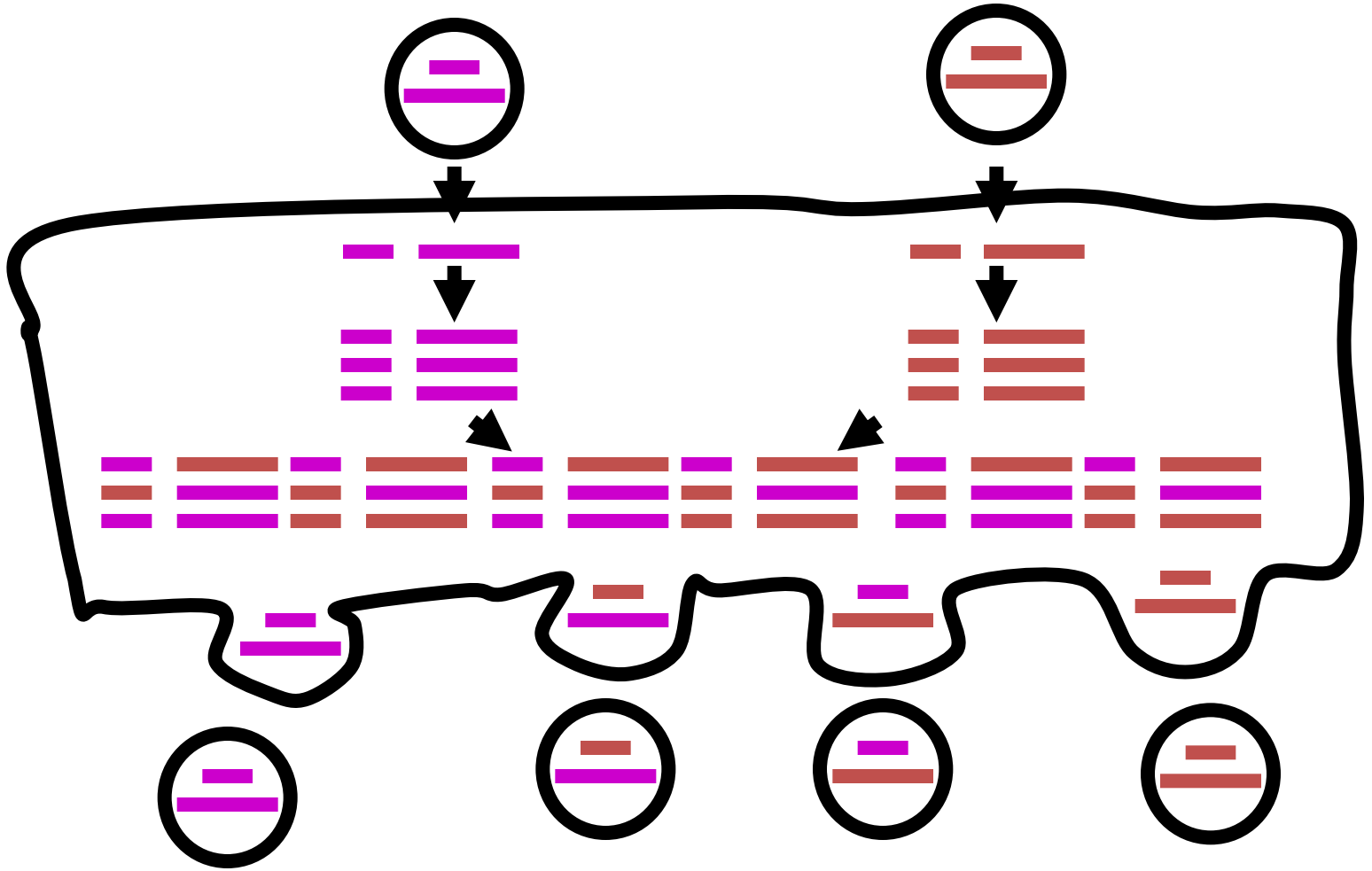
COPY CHOICE RECOMBINATION



COPY CHOICE RECOMBINATION



REASSORTMENT

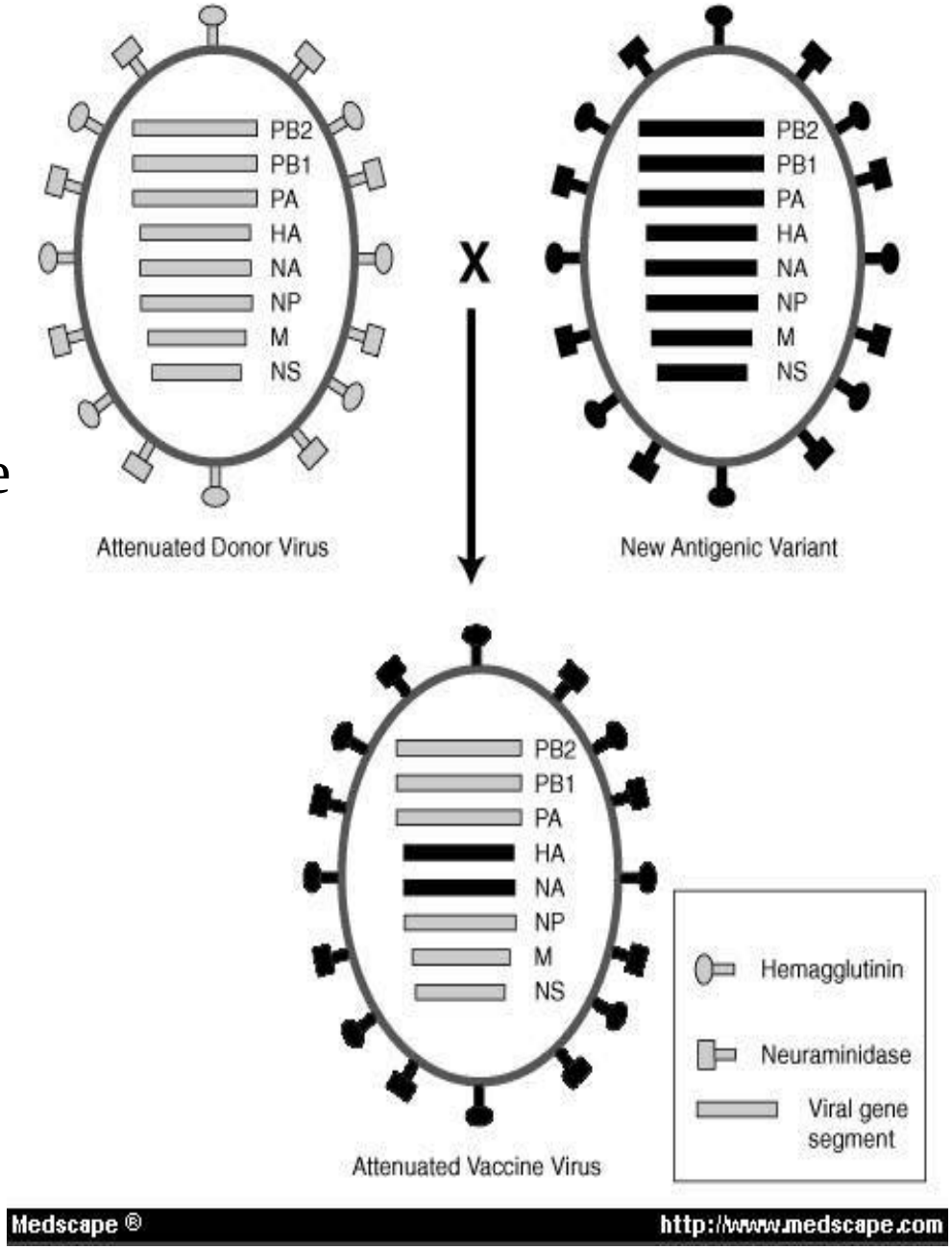


REASSORTMENT

- form of recombination (non classical)
- very efficient
- segmented viruses only
  - can occur naturally
- used in some newer vaccines
  - eg for influenza and rotaviruses

INFLUENZA VIRUS

- cold adapted
- temperature-sensitive
- attenuated
- live vaccine
- intranasal delivery
- approved 2003



adapted from Treanor JJ Infect. Med. 15:714

rotavirus vaccine (Rotateq)

- human-bovine reassortants
- live
- oral

rotavirus vaccine (Rotarix)

- attenuated human rotavirus
- live
- oral

NON-SEGMENTED NEGATIVE STRAND RNA VIRUSES

- no classical recombination
- no copy choice
- no reassortment

  – least ability to exchange genetic material

Defective viruses:

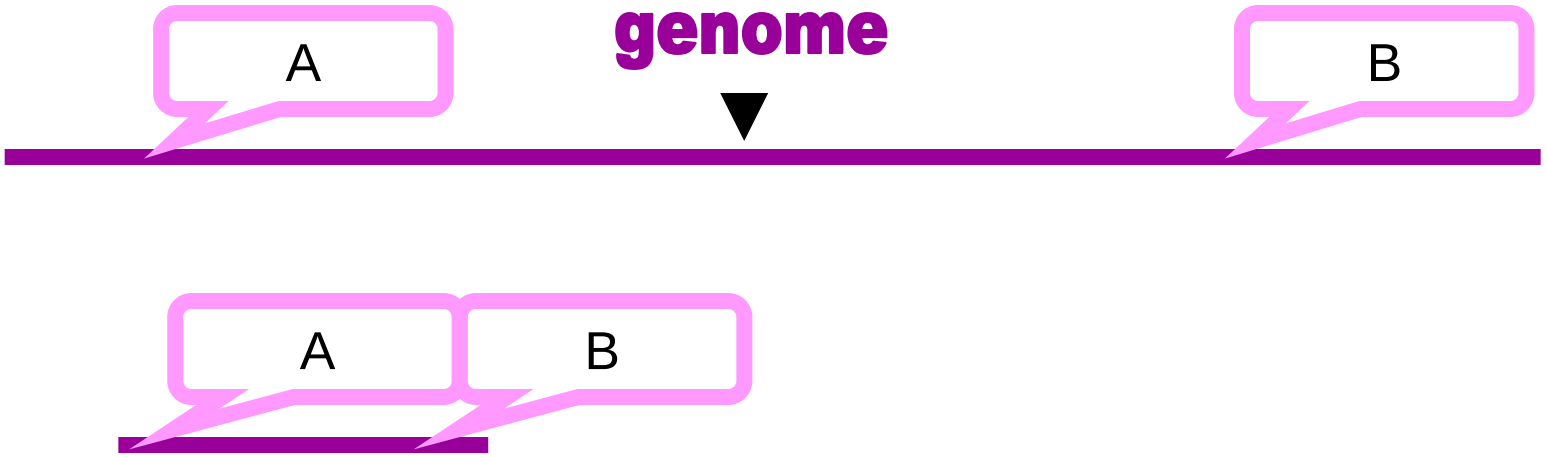
are genetically deficient and incapable of producing infectious progeny virions.

Helper virus:

can supplement the genetic deficiency and make defective viruses replicate progeny virions when they simultaneously infect host cell with defective viruses.

Defective Viruses

- Defective Viruses lack gene(s) necessary for a complete infectious cycle
- helper viruses provide missing functions



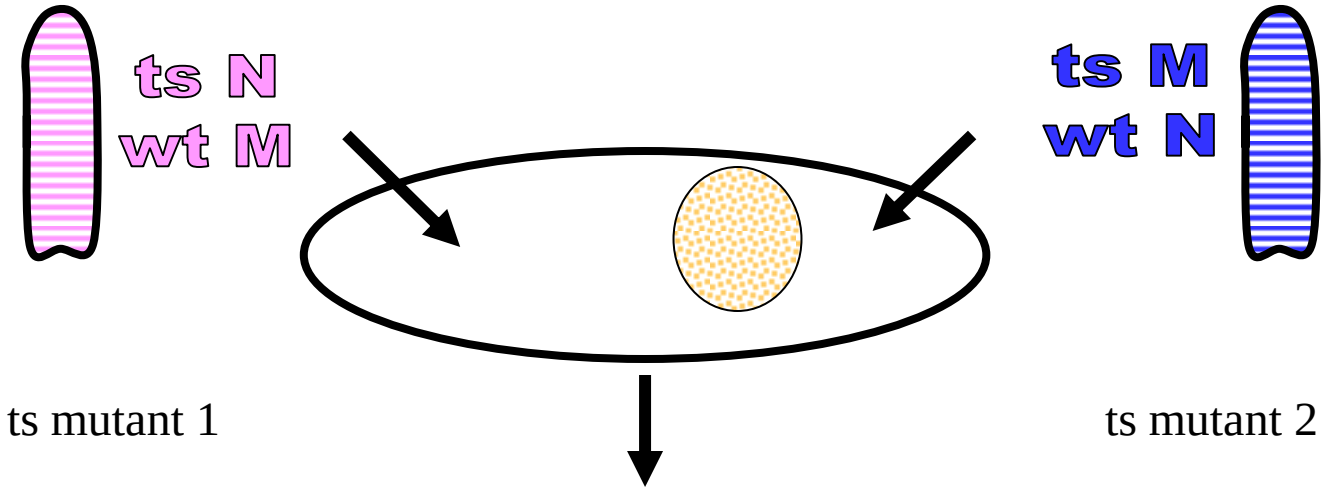
Defective interfering particles (DIP)

DIP:

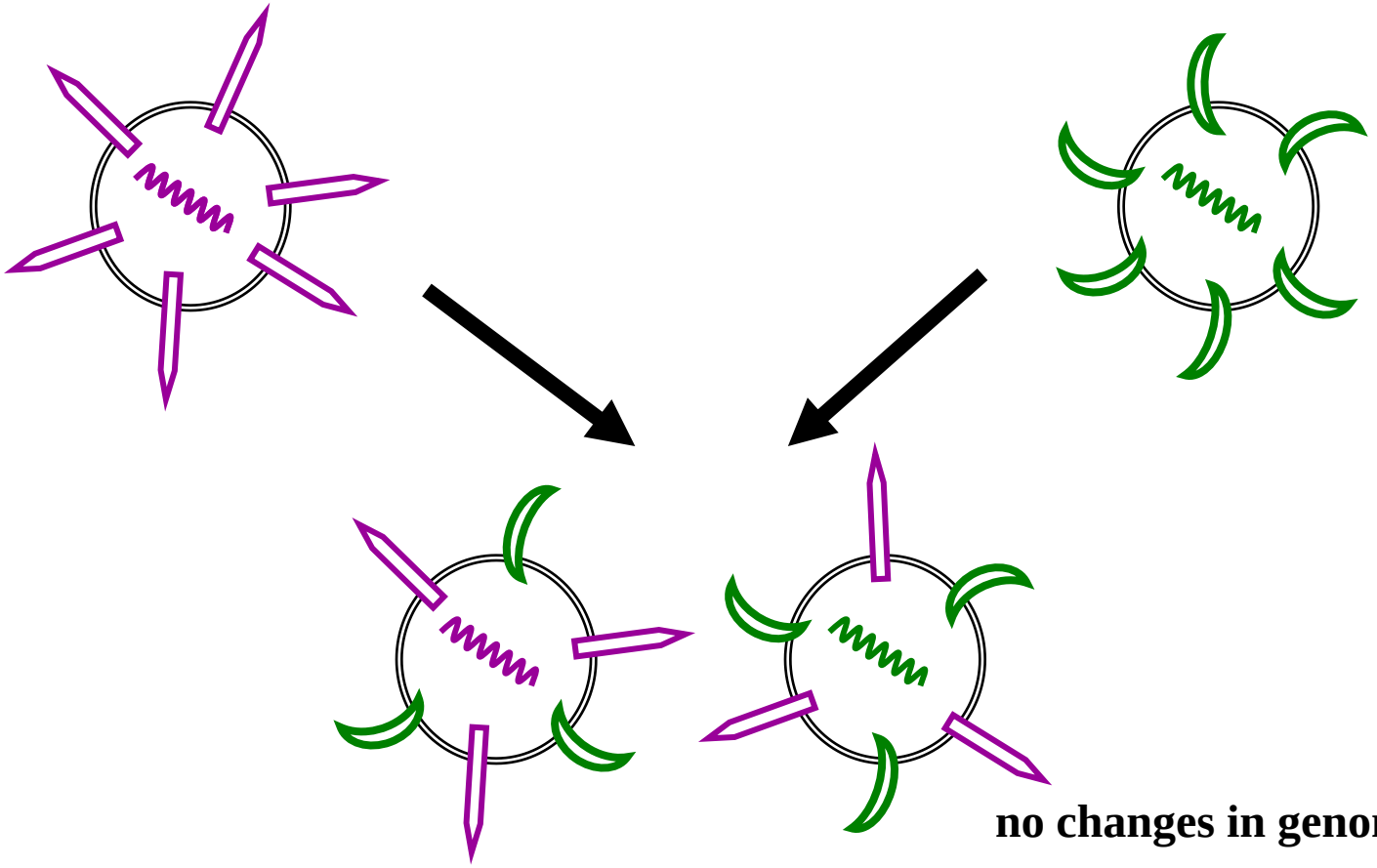
- Defective viruses which can occupy the cell machinery necessary for normal virus replication to prevent virus production, are called "defective interfering particles" (DIP).

COMPLEMENTATION

Interaction at the functional level, NOT the nucleic acid level



Progeny virus assembled using wt N and wt M proteins
Genomes in progeny are either ts M or ts N



no changes in genome

possibly altered host range

possibly resistant to antibody neutralization