Origin and dissemination mechanisms of antibiotic resistance

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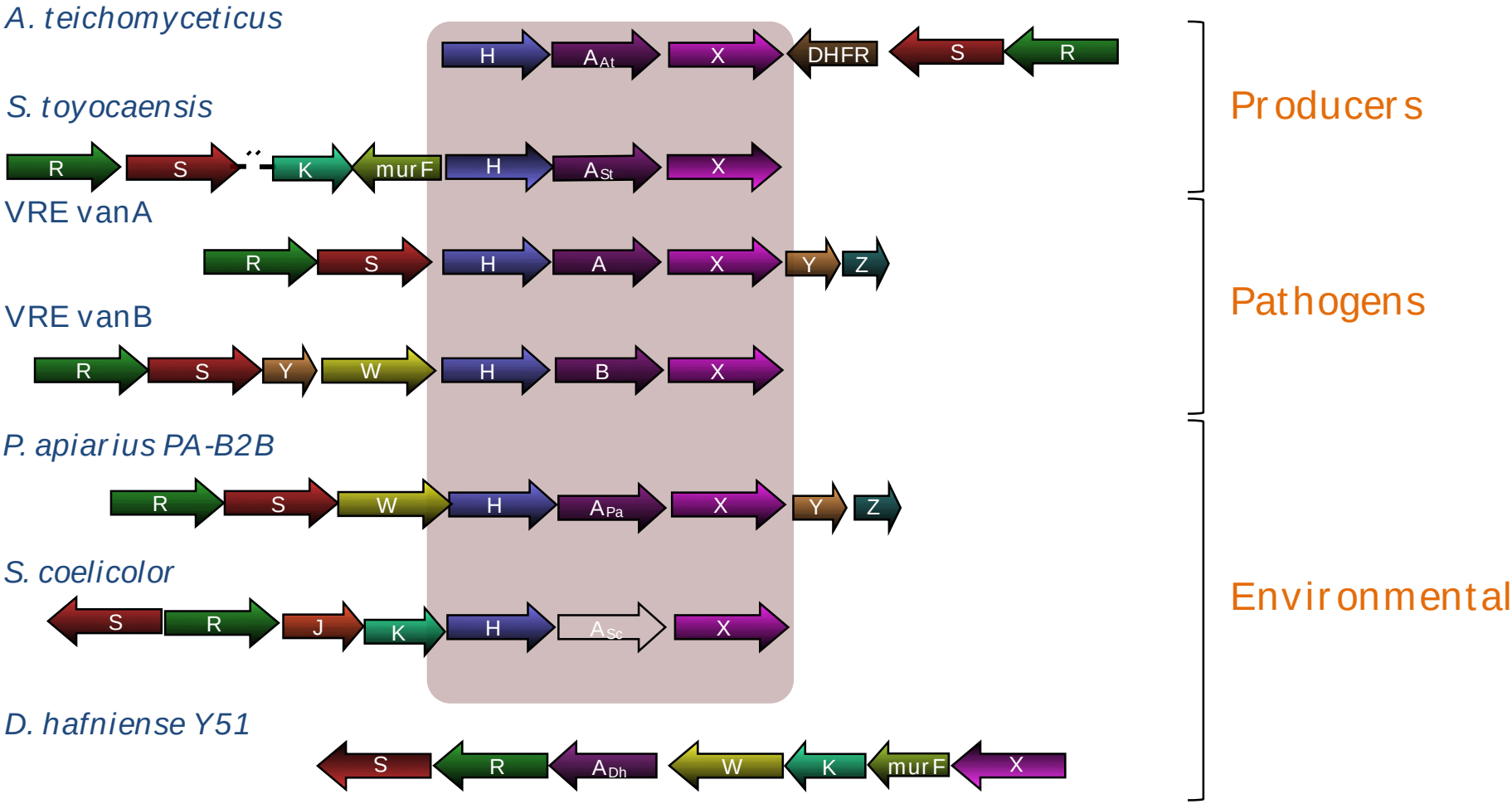
Outline

Origin
- in antibiotic producers
- in susceptible environmental bacteria

Horizontal gene transfer
- Plasmids
- Transposons
- ICE
- Antibiotic induced HGT

Mutations
- Antibiotic induced mutations
- Horizontal mutation transfer
- Antibiotic induced mutation transfer

Vancomycin Resistance Distribution



Kalan *et al*. 2009. Antimicrob. Agents Chemother. **53**:2841-5

Aminoglycoside 3'-*O*-phosphotransferase type VI

- First reported the corresponding *aphA6* gene in *A. baumannii* where it is carried by self-transferable plasmids

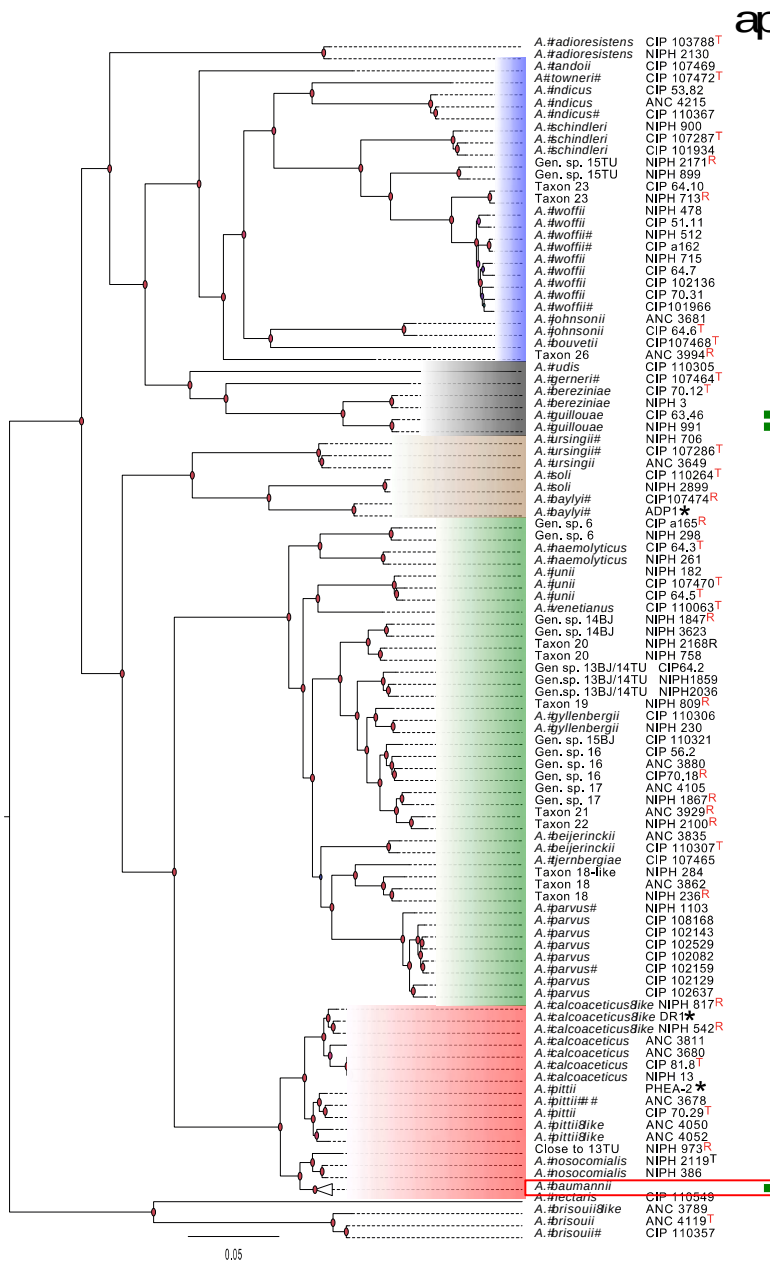
- Subsequent dissemination to *Enterobacteriaceae* and *P. aeruginosa* where it is part of Tn*1528* and Tn*aphA6* composite transposons

- Based on the:
  - low G+C % of *aphA6* (33%)
  - link with IS largely spread in *Acinetobacter* spp

➢ We suggested an origin in *Acinetobacter* spp. for the gene

Lambert *et al.* 1988. Antimicrob. Agents Chemother. **32**:15-19
Lambert *et al.* 1990. Antimicrob. Agents Chemother. **34**:1244-1248
Lambert *et al.* 1994. Antimicrob. Agents Chemother. **38**:702-706

Origin of Aph(3')-VI

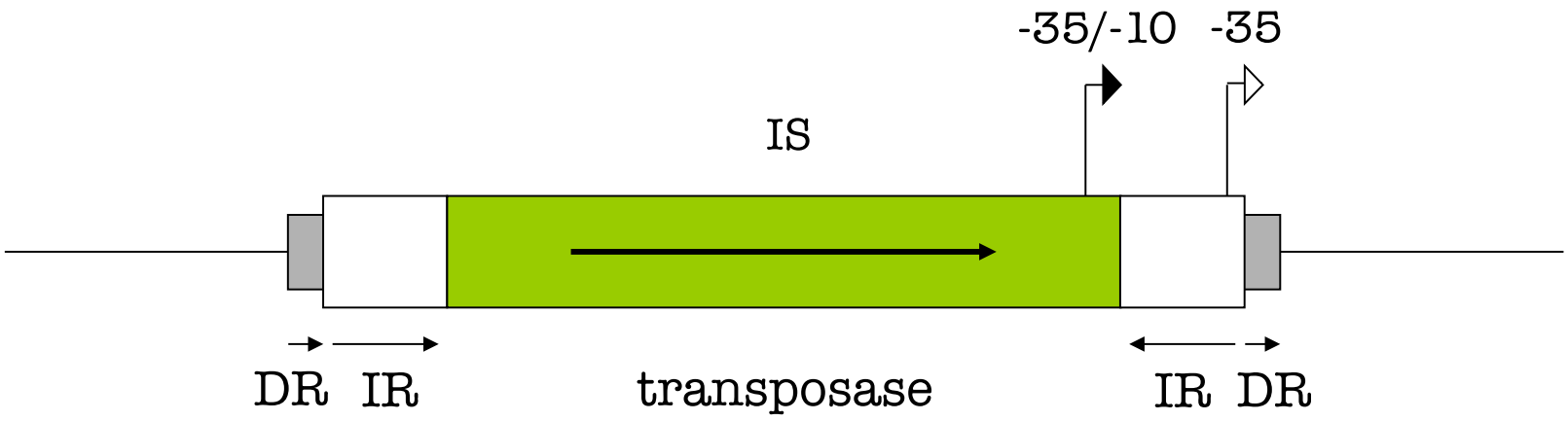


Species	Kanamycin	Amikacin	Gene
A. guillouiae	R	S	aphA6
A. guillouiae	R	S	aphA6

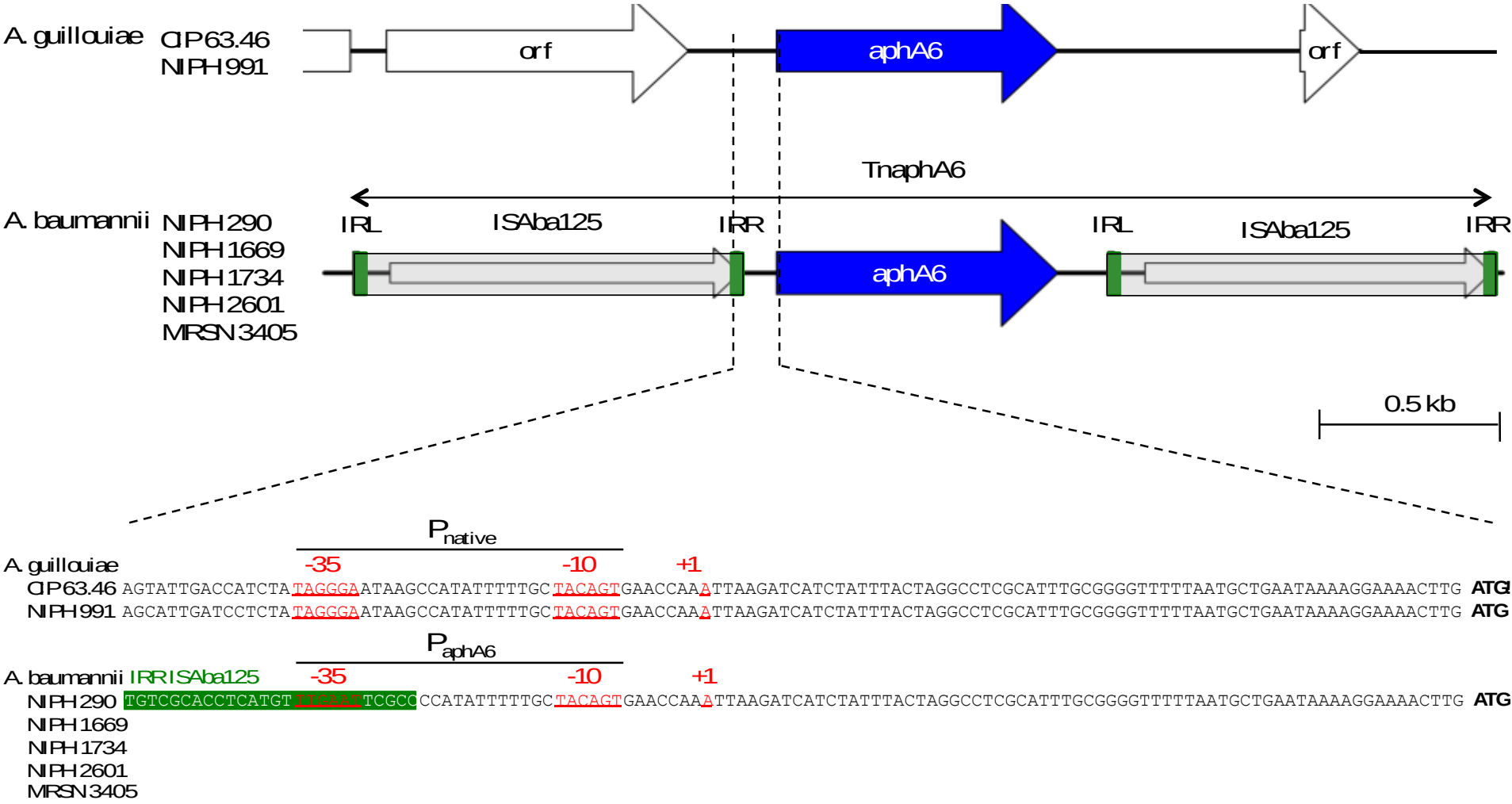
Species	Kanamycin	Amikacin	Gene
A. baumannii	R	R	aphA6

Yoon et al. 2014 mBio **5**:e01972-14

Portable promoters



Genomic environment of *aphA6*



Yoon *et al*. 2014 mBio **5**:e01972-14

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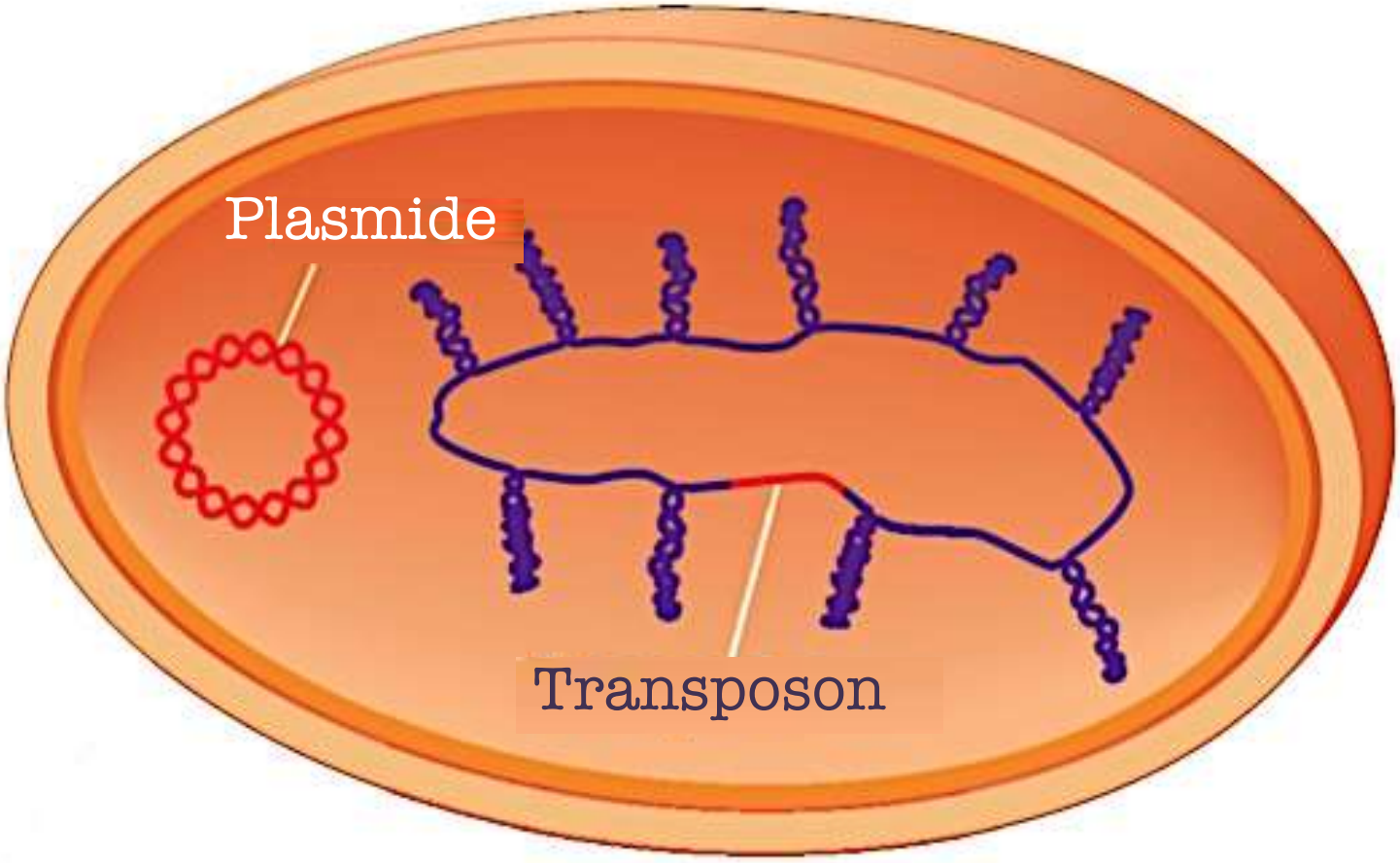
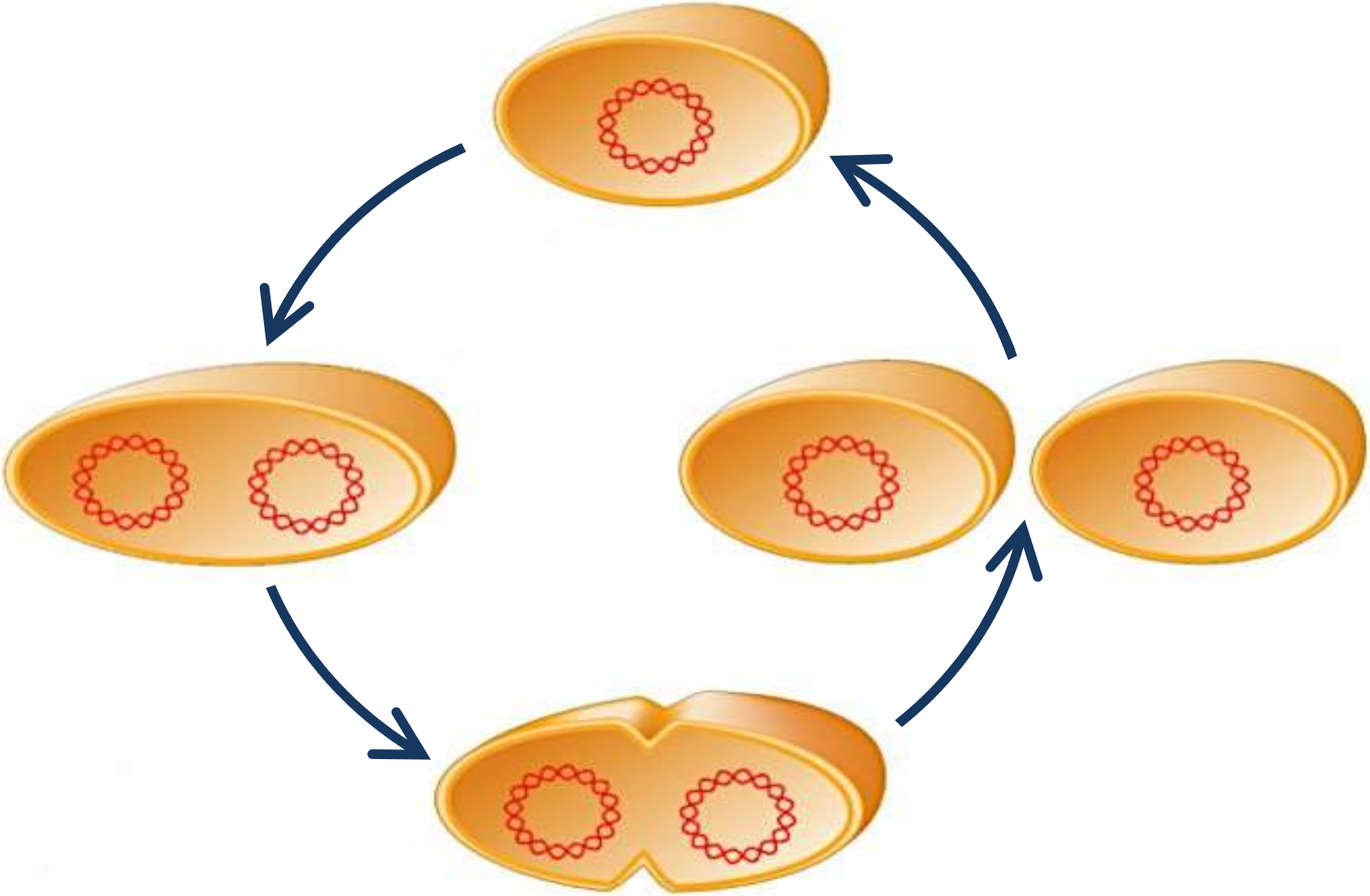
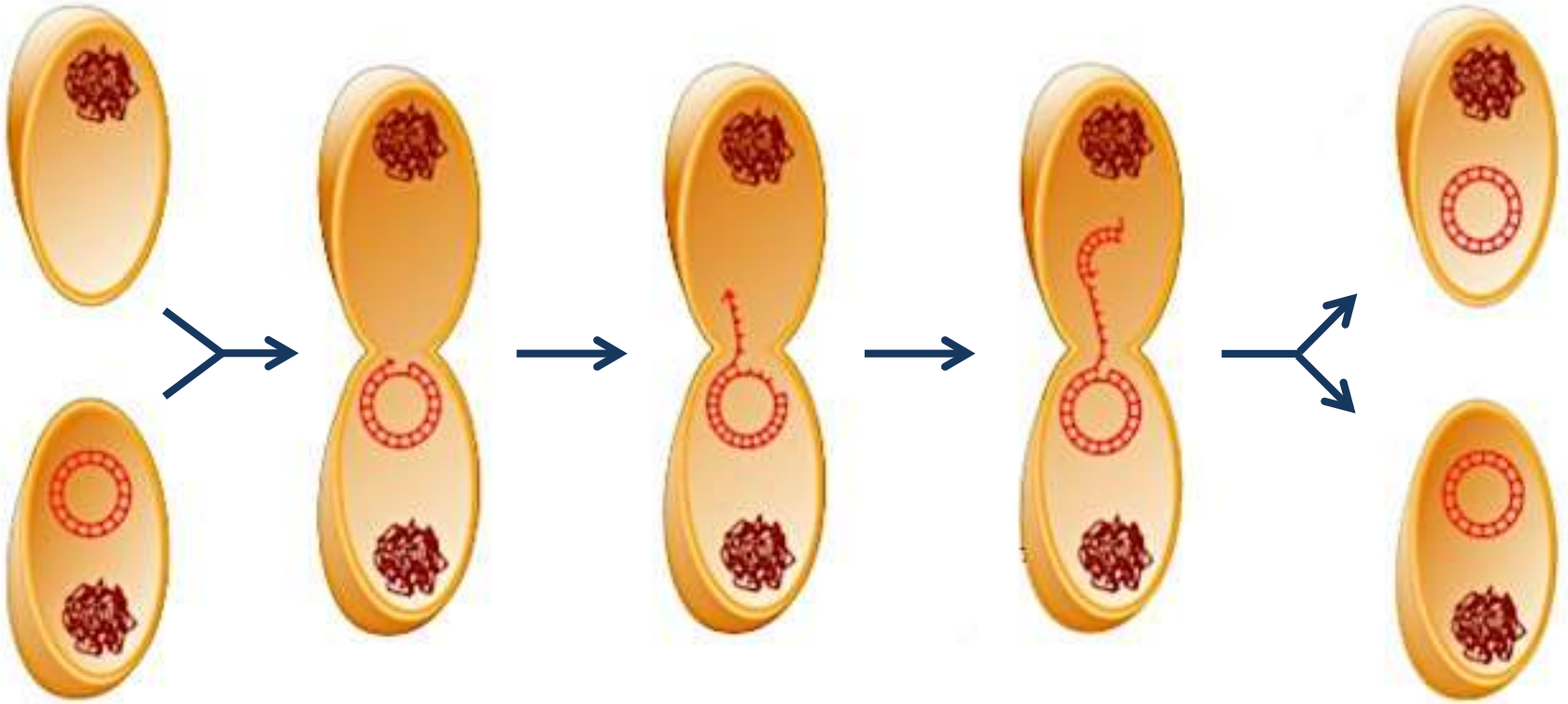
Bacterial genome



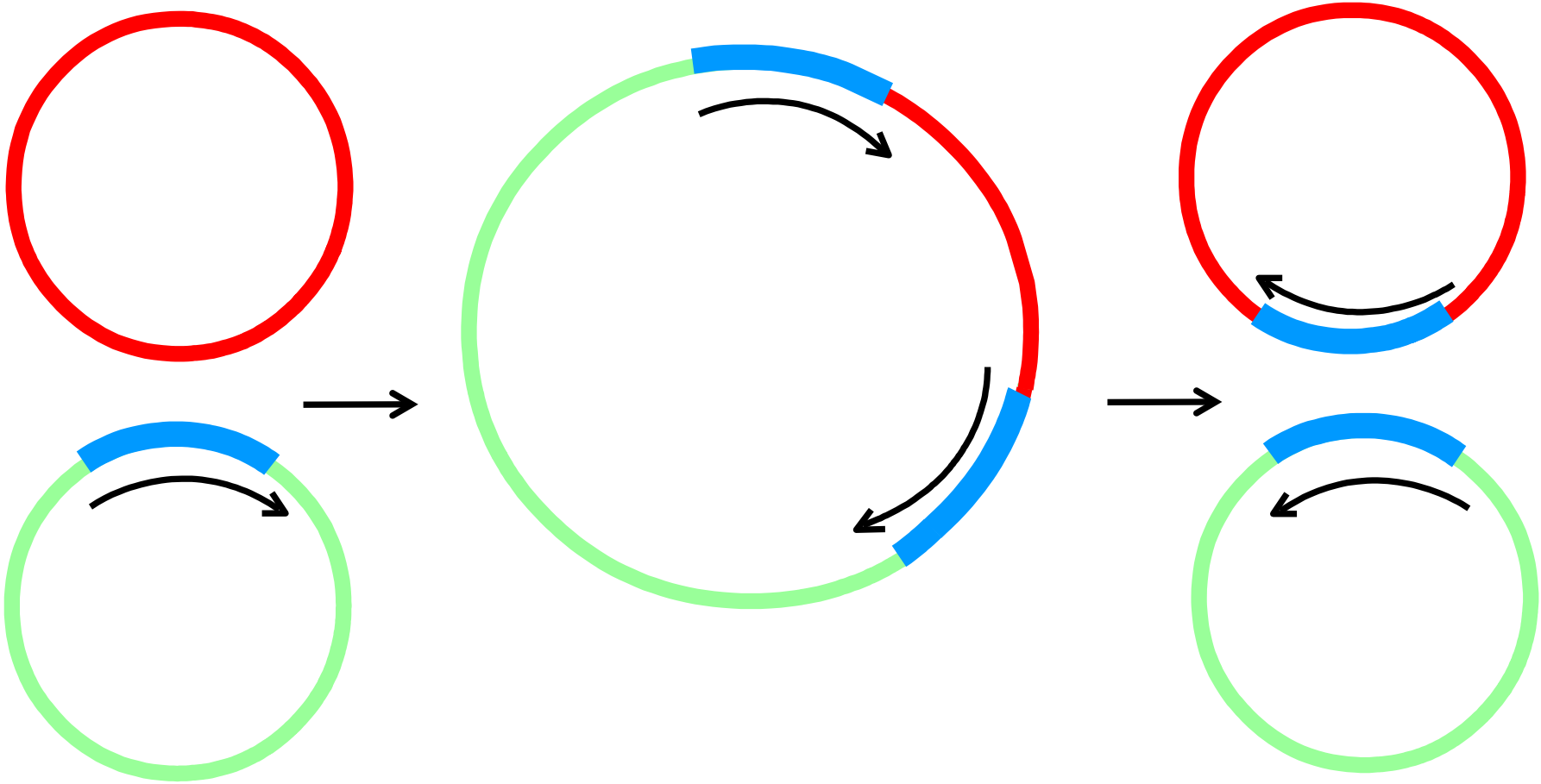
Bacterial life cycle



Plasmid transfer by conjugation



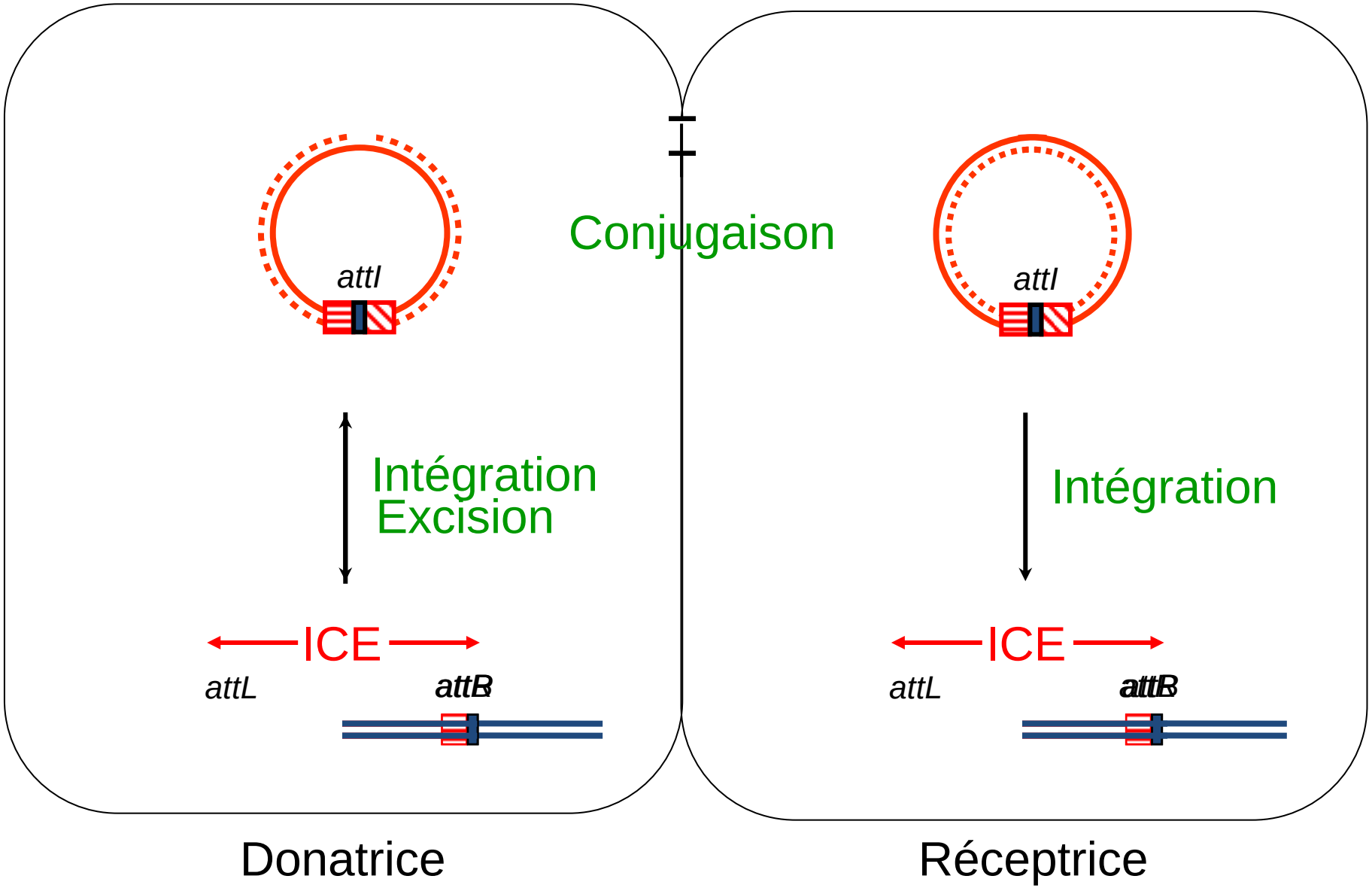
Replicative transposition



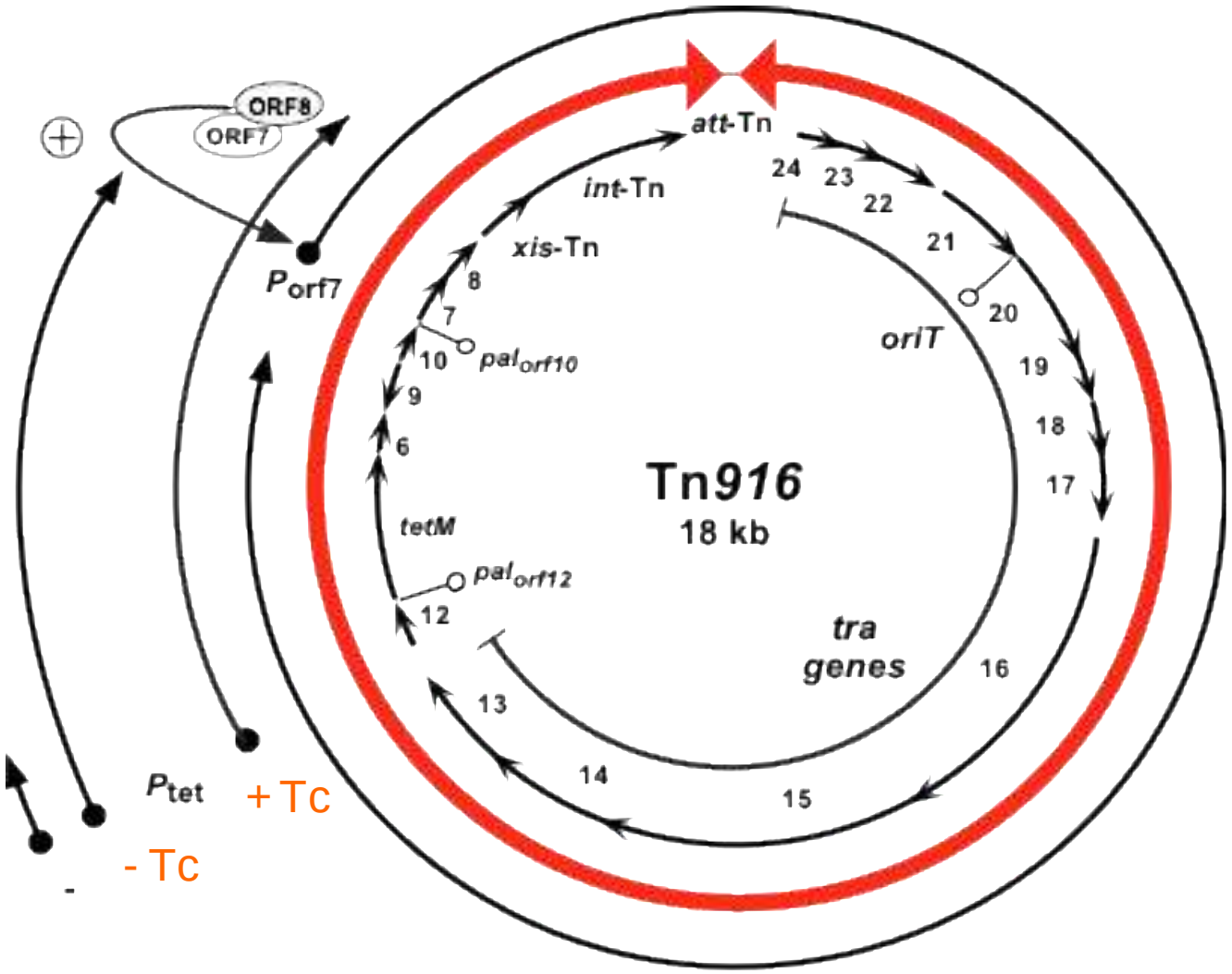
Combinatorial genetics of antibiotic resistance

Vecteur	Hôte
Bactéries	Mammifères
Plasmides	Bactéries
Transposons	Replicons

Transfert d'un Integrative Conjugative Element



Regulation of transfer to ICE by tetracycline



Manganelli *et al*. 1995. Plasmid **34**:48-57

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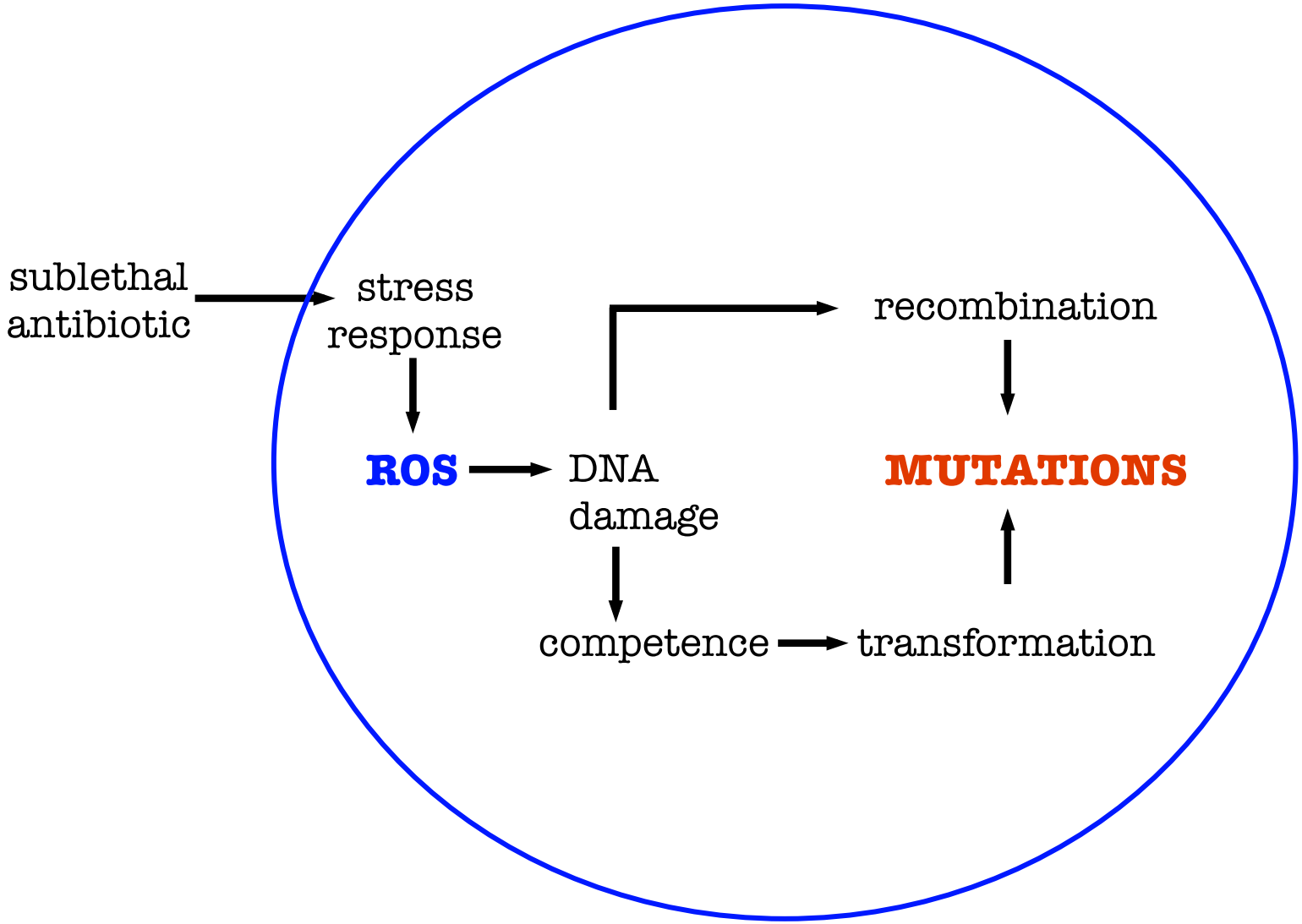
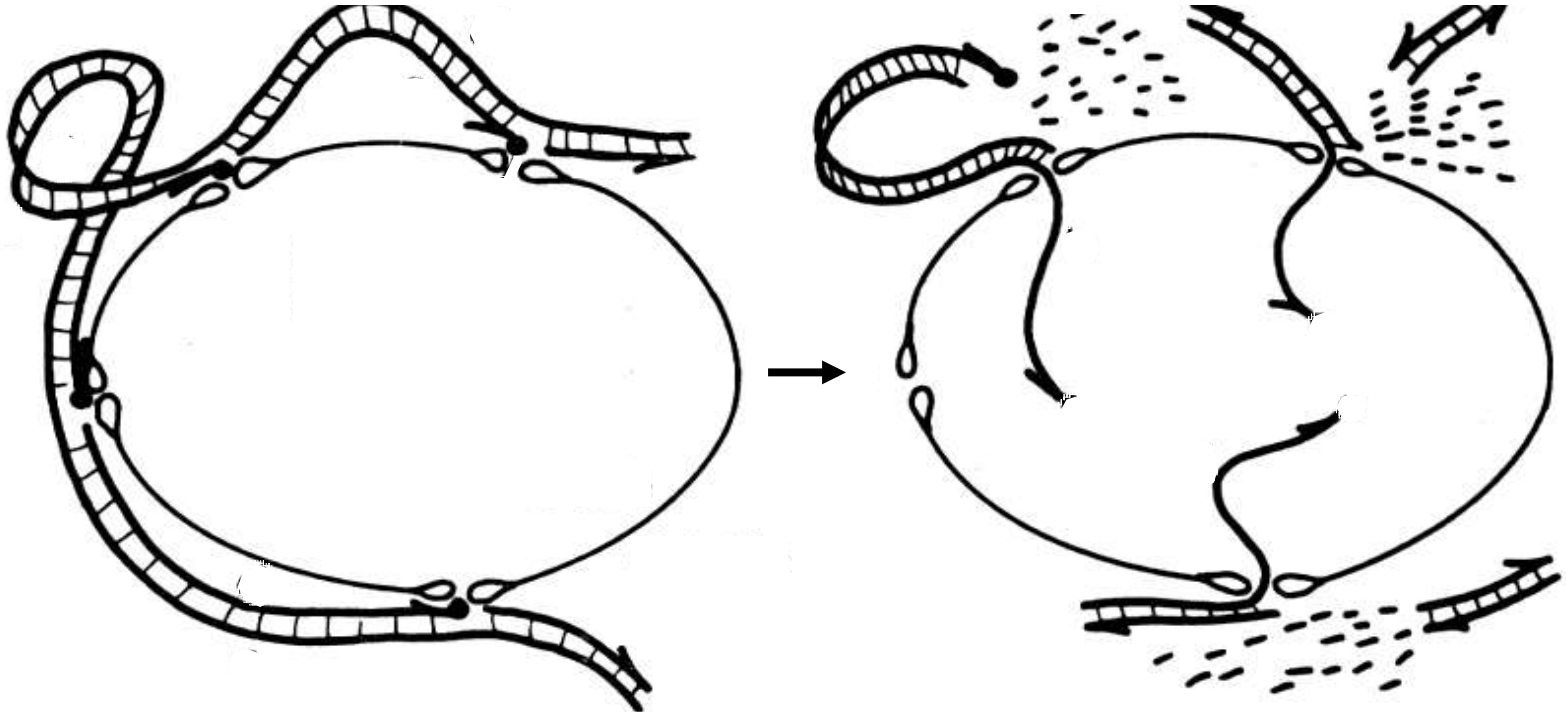
Antibiotic induced increase in mutation rate



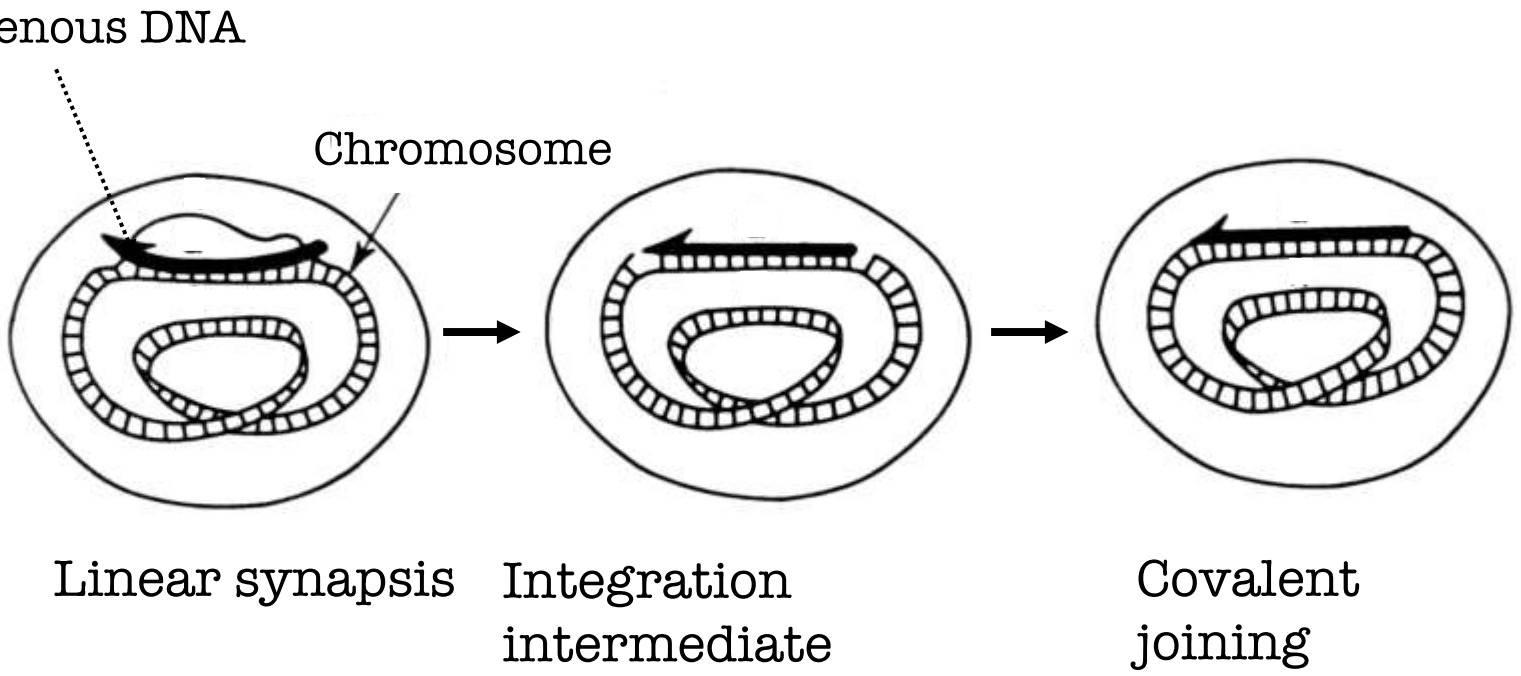
Kohanski *et al.* 2010. Mol. Cell **37**:311-20

Transformation: internalization of exogenous DNA



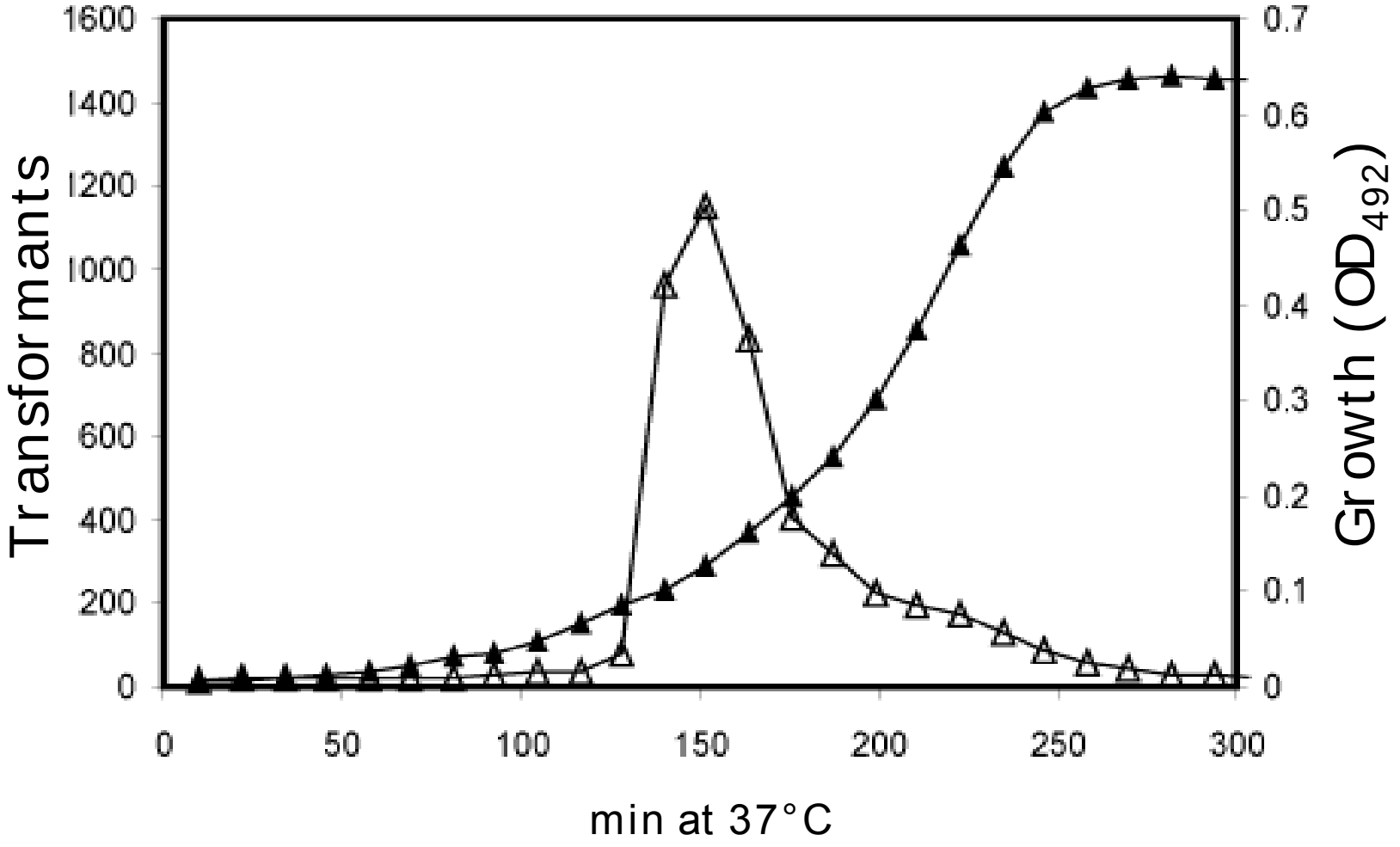
Lacks *et al.* 1967. J. Mol. Biol.

Transformation: processing of internalized DNA



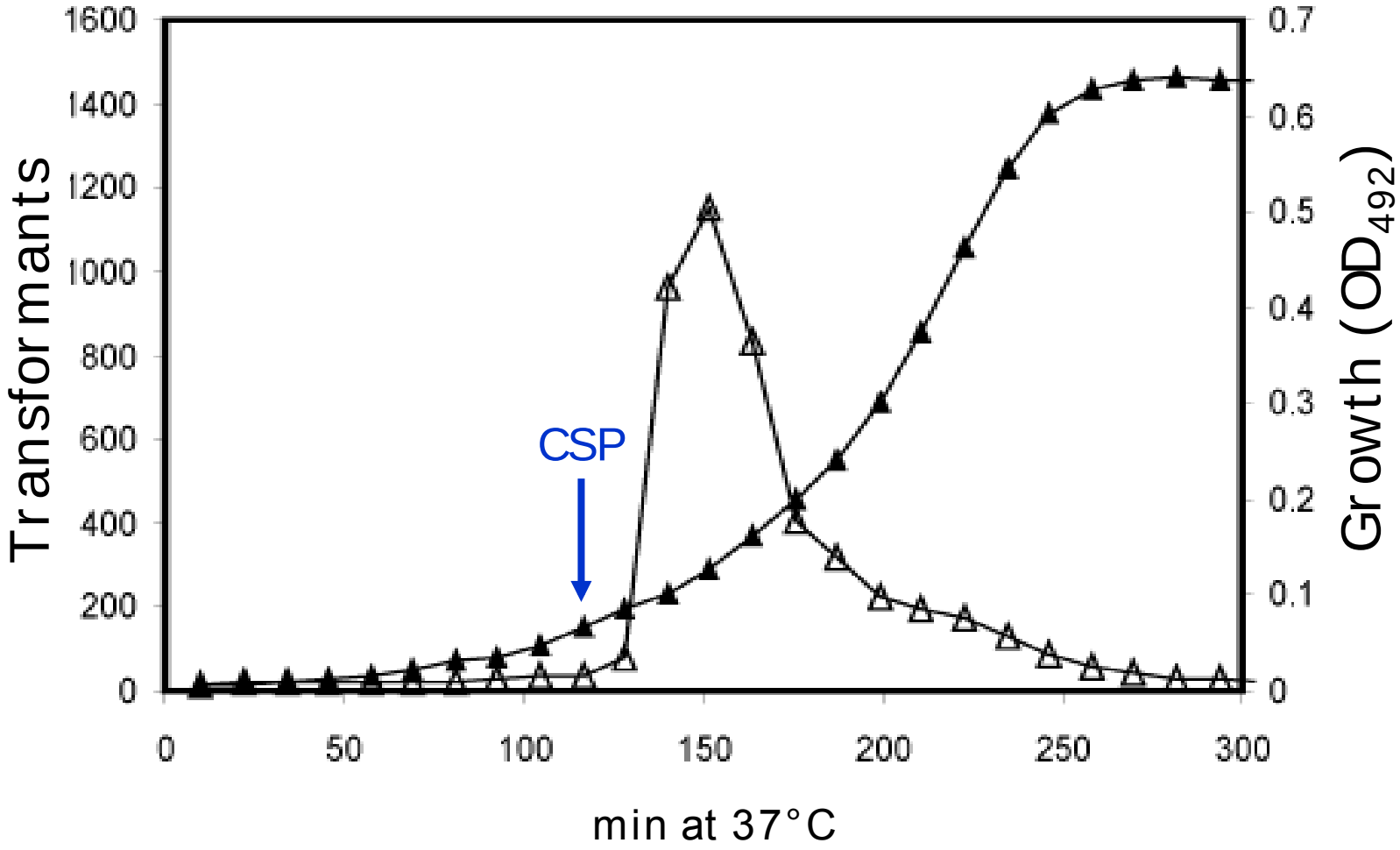
Lacks *et al.* 1967. J. Mol. Biol.

Competence for transformation is transient



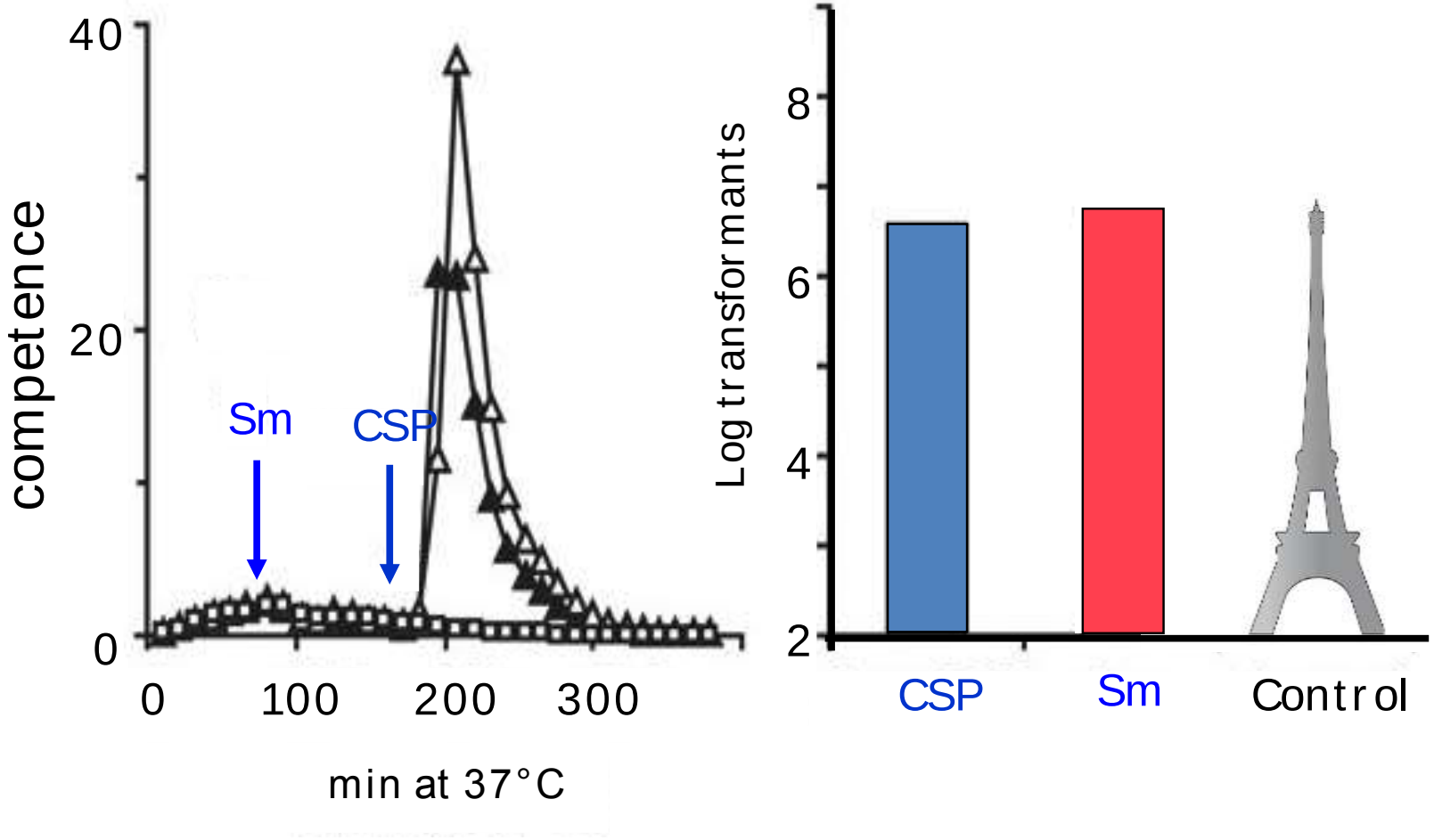
Håvarstein *et al.* 1995. Proc. Nat. Acad. Sci. USA

The Competence Stimulating Peptide (CSP) induces competence



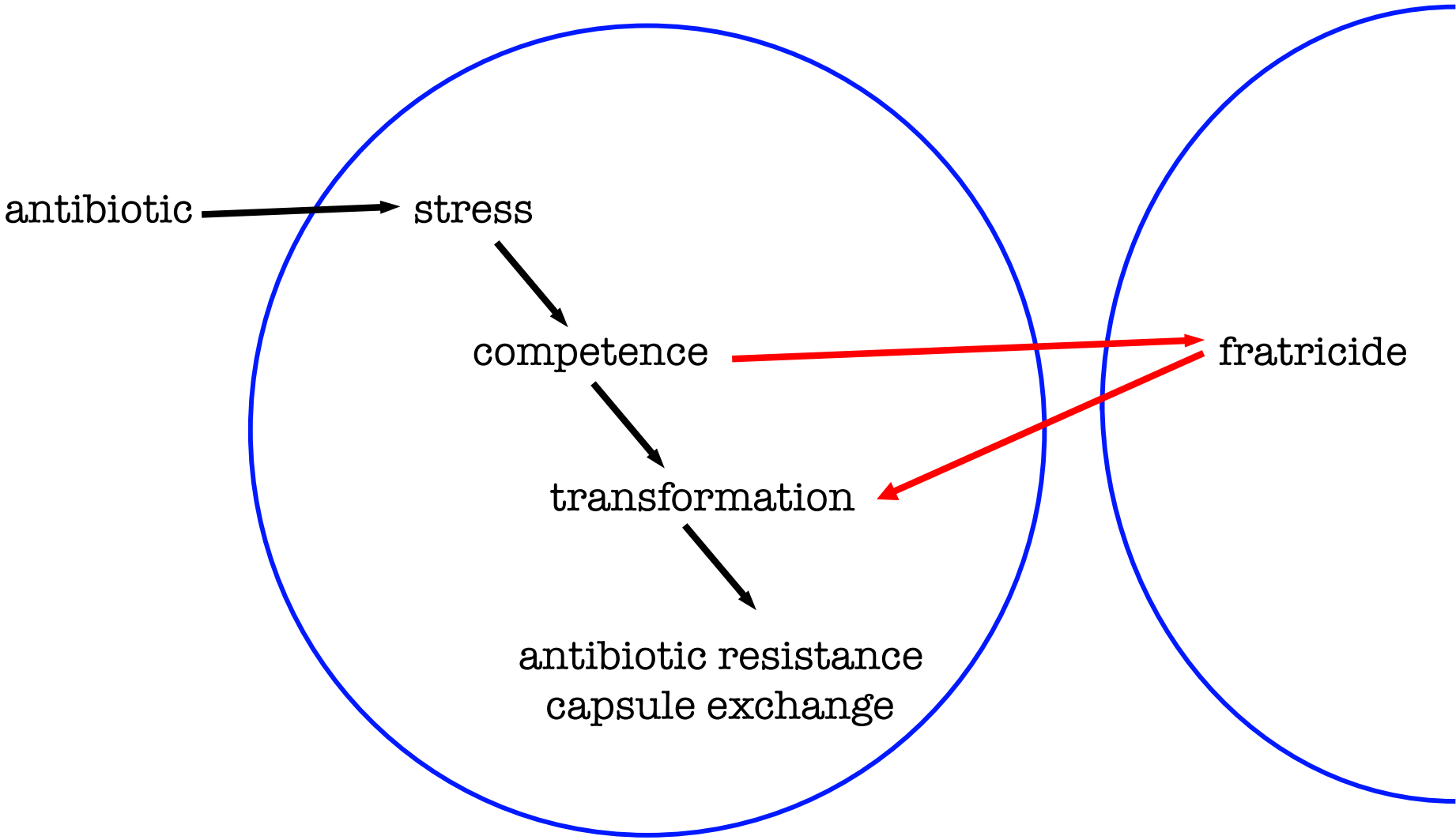
Håvarstein *et al.* 1995. Proc. Nat. Acad. Sci. USA

Induction of transformation in *S. pneumoniae*



Phrudhomme *et al*. 2006. Science

Antibiotics promote evolution of resistance



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