Genetic Basis of Variation in Bacteria

I. Organization of genetic material in bacteria
   a. chromosomes
   b. plasmids

II. Genetic variation: Source
    a. point mutations
    b. DNA rearrangements

III. Genetic variation: Transmission
     a. transformation
     b. transduction
     c. conjugation

IV. Genetic variation: Implications for pathogenesis
Genetic basis of variation: Griffiths (1928)

Organization of genetic material in bacteria: chromosomes

- Most bacteria contain a single chromosome (+ extrachromosomal elements)
- Some bacteria have been found also to contain 2-3 replicons which can be considered either megaplasmids or minichromosomes e.g. 3.0 Mb and 0.9 Mb replicons in Rhodobacter sphaeroides
- A few bacterial genera contain >1 chromosome e.g. 2.1 Mb and 1.2 Mb chromosomes in Brucella
- Some bacteria harbour large replicons essential for survival in a specific ecological niche but not under laboratory conditions e.g. 1.4 Mb and 1.7 Mb replicons in Rhizobium meliloti are required for plant symbiosis
Organization of genetic material in bacteria: plasmids

- Extrachromosomal
- Circular or linear
- 2 kb to hundreds of kb in size
- Non-essential
- May carry ‘supplemental’ genetic information or may be cryptic
- Employ host functions for most of DNA metabolism

Examples of naturally-occuring plasmids and relevant features

<table>
<thead>
<tr>
<th>Plasmid</th>
<th>Host</th>
<th>Plasmid size (kb)</th>
<th>Relevant feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT181</td>
<td>Staphylococcus aureus</td>
<td>4.4</td>
<td>Tetracycline resistance</td>
</tr>
<tr>
<td>ColE1</td>
<td>Escherichia coli</td>
<td>6.6</td>
<td>Colicin production and immunity</td>
</tr>
<tr>
<td>pAM1</td>
<td>Enterococcus faecalis</td>
<td>26.0</td>
<td>Erythromycin resistance</td>
</tr>
<tr>
<td>pAM72</td>
<td>Enterococcus faecalis</td>
<td>48.4</td>
<td>Methicillin resistance</td>
</tr>
<tr>
<td>pSB4010</td>
<td>Enterococcus faecalis</td>
<td>53.8</td>
<td>mRNA precursor</td>
</tr>
<tr>
<td>pSB51</td>
<td>Enterococcus faecalis</td>
<td>28.0</td>
<td>Metal ion resistance</td>
</tr>
<tr>
<td>pC107</td>
<td>Escherichia coli subsp.</td>
<td>53.8</td>
<td>Structural determinant</td>
</tr>
<tr>
<td>pR671</td>
<td>Yersinia pseudotuberculosis</td>
<td>150.8</td>
<td>Yersinia determinants</td>
</tr>
<tr>
<td>pR672</td>
<td>Pseudomonas aeruginosa</td>
<td>158.6</td>
<td>Ammonium (ammonium) oxidase</td>
</tr>
<tr>
<td>pK1203</td>
<td>Pseudomonas aeruginosa</td>
<td>167.8</td>
<td>Aromatic hydrocarbon degradation</td>
</tr>
<tr>
<td>pB2050</td>
<td>Bacillus thuringiensis subsp.</td>
<td>172.7</td>
<td>Mosquito larval toxin</td>
</tr>
<tr>
<td>pP701</td>
<td>Bacillus subtilis</td>
<td>181.0</td>
<td>Phage production</td>
</tr>
<tr>
<td>pAM100</td>
<td>Chalconasin aurogenin</td>
<td>184.6</td>
<td>Pseudomonas aeroginosa</td>
</tr>
<tr>
<td>pP62</td>
<td>Enterococcus faecalis</td>
<td>189.3</td>
<td>Functions associated with plant symbiosis</td>
</tr>
</tbody>
</table>

Sources of genetic variation: point mutations

- Transitions
  - Purine: G → A, C → T
  - Pyrimidine: T → C, G → A
- Transversions
  - Purine: G → T, C → A
  - Pyrimidine: T → C, G → A

There are four types of transitions
There are eight types of transversions
Sources of genetic variation: point mutations

Mutation phenotypes

- Silent mutation (synonymous): no change in amino acid
  \[\text{AAG} \rightarrow \text{AAG}\] both codes specify Arginine.
- Missense mutation (replacement: non-synonymous), change in amino acid:
  - Non-synonymous: missense or altered replacement
    \[\text{UUU (Pha)} \rightarrow \text{UUC (Ser)}\] Pha is hydrophobic and Ser is polar.
- Nonsense mutation, premature termination of translation:
  \[\text{CA6 (Gin)} \rightarrow \text{UA6 (Stop)}\]
- Frameshift: addition or deletion of base pairs, not in a multiple of three, within the coding region of a gene.

Sources of genetic variation: DNA rearrangements

Insertion sequence (IS) elements:

1. Simplest type of transposable element found in bacterial chromosomes and plasmids.
2. Encode only genes for mobilization and insertion.
3. Range in size from 768 bp to 5 kb.
4. IS1 first identified in E. coli's galactose operon is 768 bp long and is present with 4-19 copies in the E. coli chromosome.
5. Ends of all known IS elements show inverted terminal repeats (ITRs).

Sources of genetic variation: DNA rearrangements

Integration of IS element in chromosomal DNA.

Sources of genetic variation: DNA rearrangements

Sources of genetic variation: frequency of occurrence

High frequency → Low diversity
Low frequency → High diversity

* As frequency per cell per generation
Transmission of genetic variation: Luria-Delbruck test

1. Resistance by mutation is a physiological response

2. Resistance by mutation arises randomly in time

Results fit with expectations if random mutation occur at random.

Transmission of genetic variation: mechanisms

- Transformation
  - Lysis of donor cell releases DNA into medium.
- Conjugation
  - Donor cell donates DNA to recipient cell.
- Transduction
  - Bacteriophage infects a cell.
  - Donor DNA is packaged in released phage particle and infects recipient cell.

Transmission of genetic variation: Linear transmission

- Point mutations
  - DNA rearrangement
  - Fig. 6: Chain variation.

Transmission of genetic variation: Horizontal transmission

- Transformation
- Conjugation
- Transduction
  - Fig. 3 (p.41f). Variation by means of genetic information.
Transmission of genetic variation: mechanisms

Transmission of genetic variation: antibiotic resistance

Transmission of genetic variation: transformation

Gene transfer resulting from the uptake of DNA from a donor.
Factors affecting transformation
- DNA size and state
- Sensitive to nucleases
- Competence of the recipient (Bacillus, Haemophilus, Neisseria, Streptococcus)
- Competence factor
- Induced competence

Fig. 1. Antibiotic resistance profiling of 480 soil-derived bacterial isolates
How did Zinder and Lederberg prove that the phenotype was the result of transduction?

- presence of DNAase rules out transformation
- filter prevented contact so no conjugation
- reducing filter pore size to below size of phage inhibited
There are two types of transduction:

- **generalized transduction**: A DNA fragment is transferred from one bacterium to another by a lytic bacteriophage that is now carrying donor bacterial DNA due to an error in maturation during the lytic life cycle.

- **specialized transduction**: A DNA fragment is transferred from one bacterium to another by a temperate bacteriophage that is now carrying donor bacterial DNA due to an error in spontaneous induction during the lysogenic life cycle.

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1. A lytic bacteriophage adsorbs to a susceptible bacterium.
2. The bacteriophage genome enters the bacterium. The genome directs the bacterium’s metabolic machinery to manufacture bacteriophage components and enzymes.
3. Occasionally, a bacteriophage head or capsid assembles around a fragment of donor bacterium’s nucleoid or around a plasmid instead of a phage genome by mistake.
4. The bacteriophages are released.
5. The bacteriophage carrying the donor bacterium’s DNA adsorbs to a recipient bacterium.
6. The bacteriophage inserts the donor bacterium’s DNA it is carrying into the recipient bacterium.
7. The donor bacterium’s DNA is exchanged for some of the recipient’s DNA.
1. A temperate bacteriophage adsorbs to a susceptible bacterium and injects its genome.

2. The bacteriophage inserts its genome into the bacterium’s nucleoid to become a prophage.

3. Occasionally during spontaneous induction, a small piece of the donor bacterium’s DNA is picked up as part of the phage genome in place of some of the phage DNA which remains in the bacterium’s nucleoid.

4. As the bacteriophage replicates, the segment of bacterial DNA replicates as part of the phage’s genome. Every phage now carries that segment of bacterial DNA.

5. The bacteriophage adsorbs to a recipient bacterium and injects its genome.

6. The bacteriophage genome carrying the donor bacterial DNA inserts into the recipient bacterium’s nucleoid.