

Introduction to Gut Microbiota



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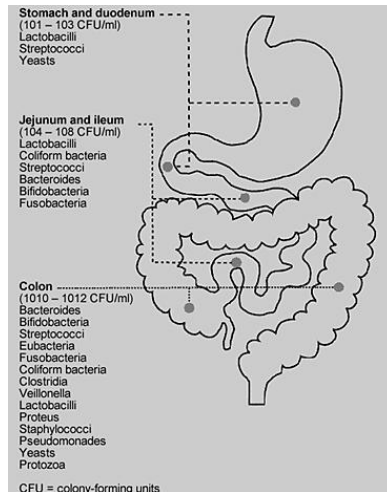
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The Bacteria in our Intestines

- **Who are they?**
 - *They outnumber us!*
- **What are they doing?**
 - *And what is their impact on our health?*
- **What determines the bacterial composition?**
 - *The intestinal ecosystem*
- **How do we study them?**
 - *Methods for gut microbiota analysis*

Intestinal microbiota

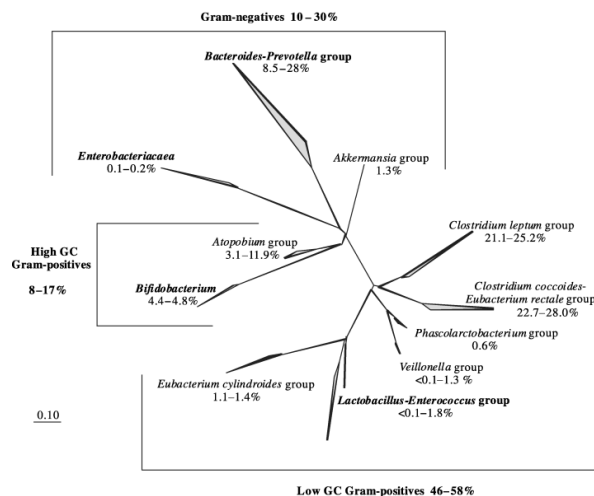


**10¹⁴ bacteria
more than 500 different
species**

**Most of these are not
cultured**

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Diversity of predominant gut species



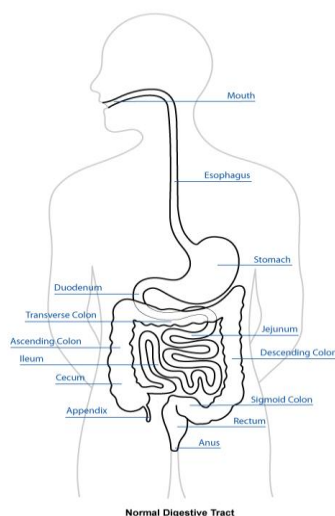
Zoetendahl, Vaughan & de Vos, 2007, Molecular Microbiology 59:1639-50

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Impact of gut microbes on host health



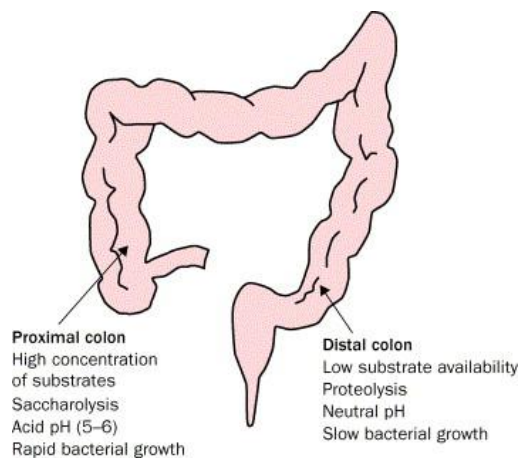
- **Immune system**
 - *Maturation/maintenance*
 - *Allergy*
 - *IBD/IBS (Crohn's, Ulcerative Colitis)*
- **Competitive exclusion of pathogens**
 - *Colonization resistance*
 - *Competition for nutrients*
 - *Competition for adhesion sites*
 - *Production of SCFA and antipathogenic substances (Lactic Acid Bacteria)*
- **Host nutrition utilization**
 - *Growth promotion*
 - *Obesity*
- **Cancer**
- **Cardiovascular diseases**

The Good, the Bad and the Ugly...

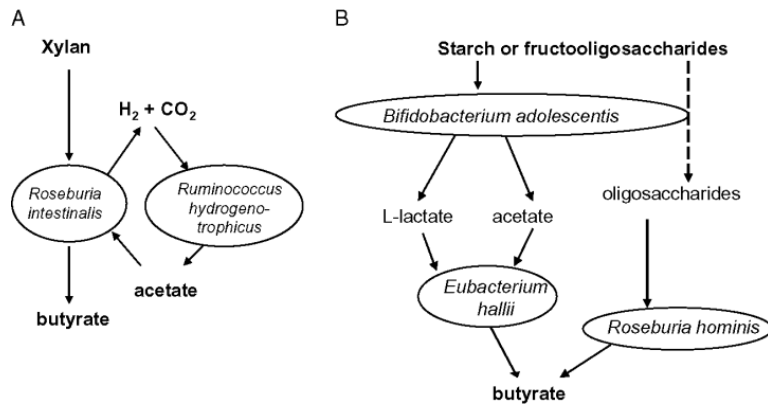
- **The good**
 - *Fermentative bacteria*
 - *Short Chain Fatty Acids, Low pH*
 - *Immune balancing*
- **The bad**
 - *Putrefactive, proteolytic*
 - *Ammonia, amines, indole, toxic enzymes*
- **The ugly**
 - *Pathogenic, infective, toxigenic*



Fermentation in the colon



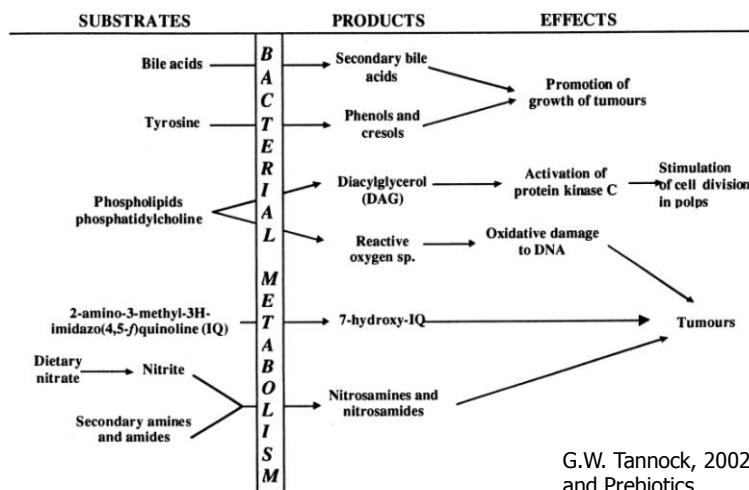
The Good: Butyrate formation



Flint et al., Environmental Microbiology Vol. 9, 5 Pages: 1101-1111

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The Bad: Carcinogen formation



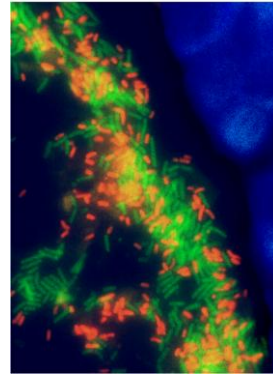
G.W. Tannock, 2002: Probiotics and Prebiotics

Figure 2. production of carcinogens and tumour promoters by the colonic microflora

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Some facts about the microbiota of the human gut

- **It is surprisingly stable**
- **Variation between individuals is much larger than variations over time**
- **Thus we all have our own 'poop-print'**



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What determines the microbiota of an individual?

- **First colonizers**

- Difference between children born by cesarian and children born through the birth channel

- **Host gene pool**

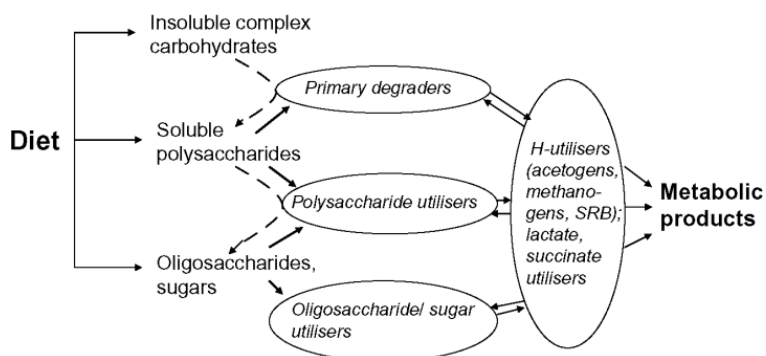
- Identical twins often have highly similar microbiotas

- **Diet**

- For adults little but probably important influence

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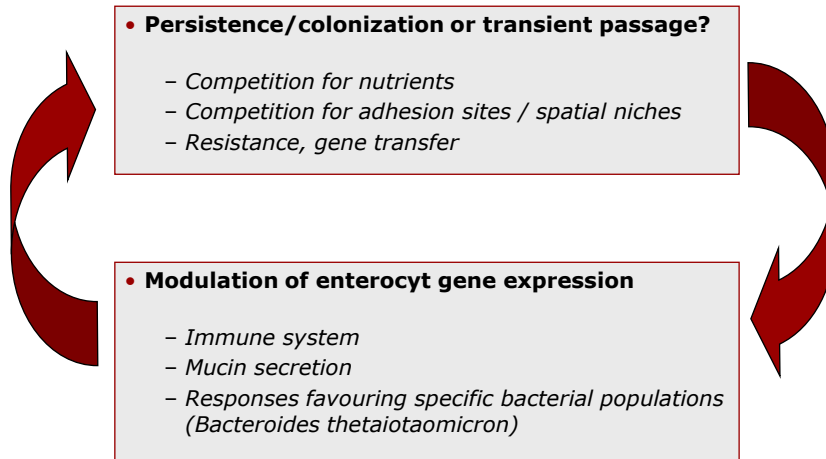
Cross feeding interactions



Flint et al., Environmental Microbiology Vol. 9, 5 Pages: 1101-1111

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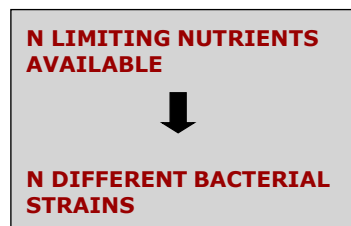
The Intestinal Ecosystem



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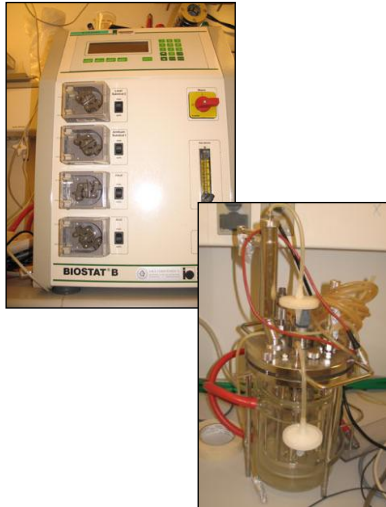
The intestine considered as a chemostat (Rolf Freter, 1983)

- $\frac{dB}{dt} = kB - uB$
 - (B : bacterial population; k : growth rate; u : excretion rate)
- k is a function of nutrient availability
- u is approximately constant
- If B is constant, then $k=u$



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Freter:

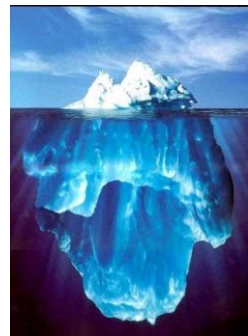


- Two bacterial strains competing for the same limiting nutrient can co-exist in the intestine only if one has specific adhesion sites available.
- Populations limited by the same nutritional compound will typically be closely related.

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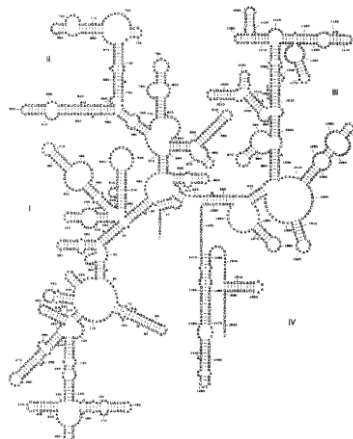
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Methods for investigation of microbial composition in complex populations

- **Selective cultivation**
 - Poor discrimination and shows only the 'tip of the iceberg'
 - Many oxygen sensitive organisms
- **16S PCR-based methods**
 - DGGE (Denaturing Gradient Gel Electrophoresis)
 - T-RFLP (Terminal Restriction Fragment Length Polymorphism)
- **Genomic-based approaches**
 - Microarrays (e.g. 16S based)
 - Metagenomic sequencing

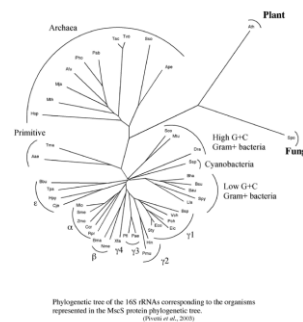
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Secondary structure of procaryotic 16S rRNA



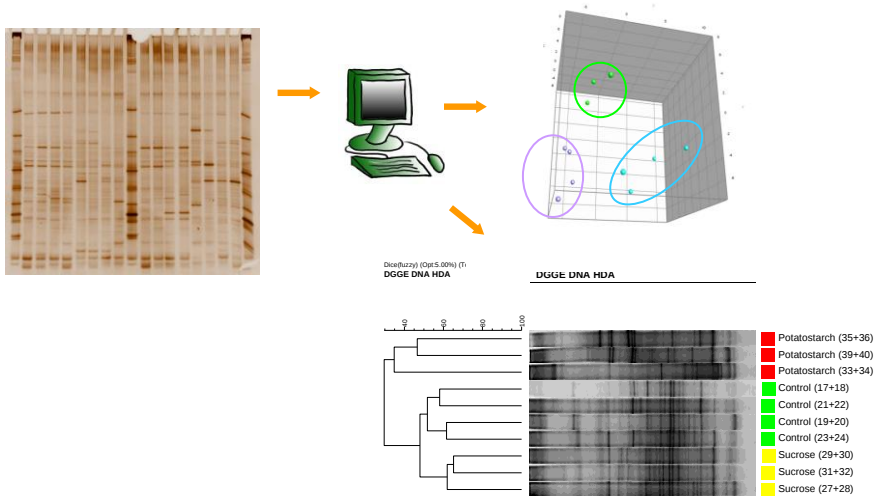
16S rRNA-based phylogenetic tree

Figure S8



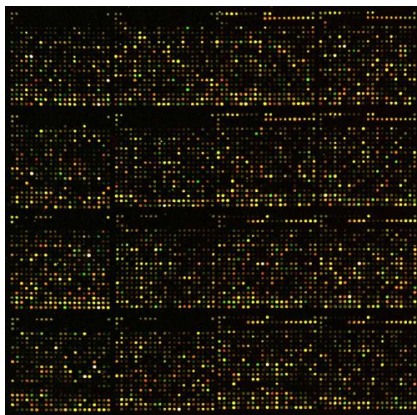
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Example: Analysis of composition of intestinal microbiota by DGGE of PCR-amplified ribosomal rRNA genes



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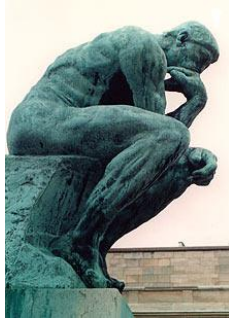
Example: Microarray analysis



- Typically 16S gene based (phylogenetic array)
- However, could also target other genes or their expression
- Data handling and analysis is essential

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...And that's THE END!



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