THURSDAY, DECEMBER 11, 2014

MICROBIAL DYSBIOSIS – A PERSONAL CARE PERSPECTIVE.

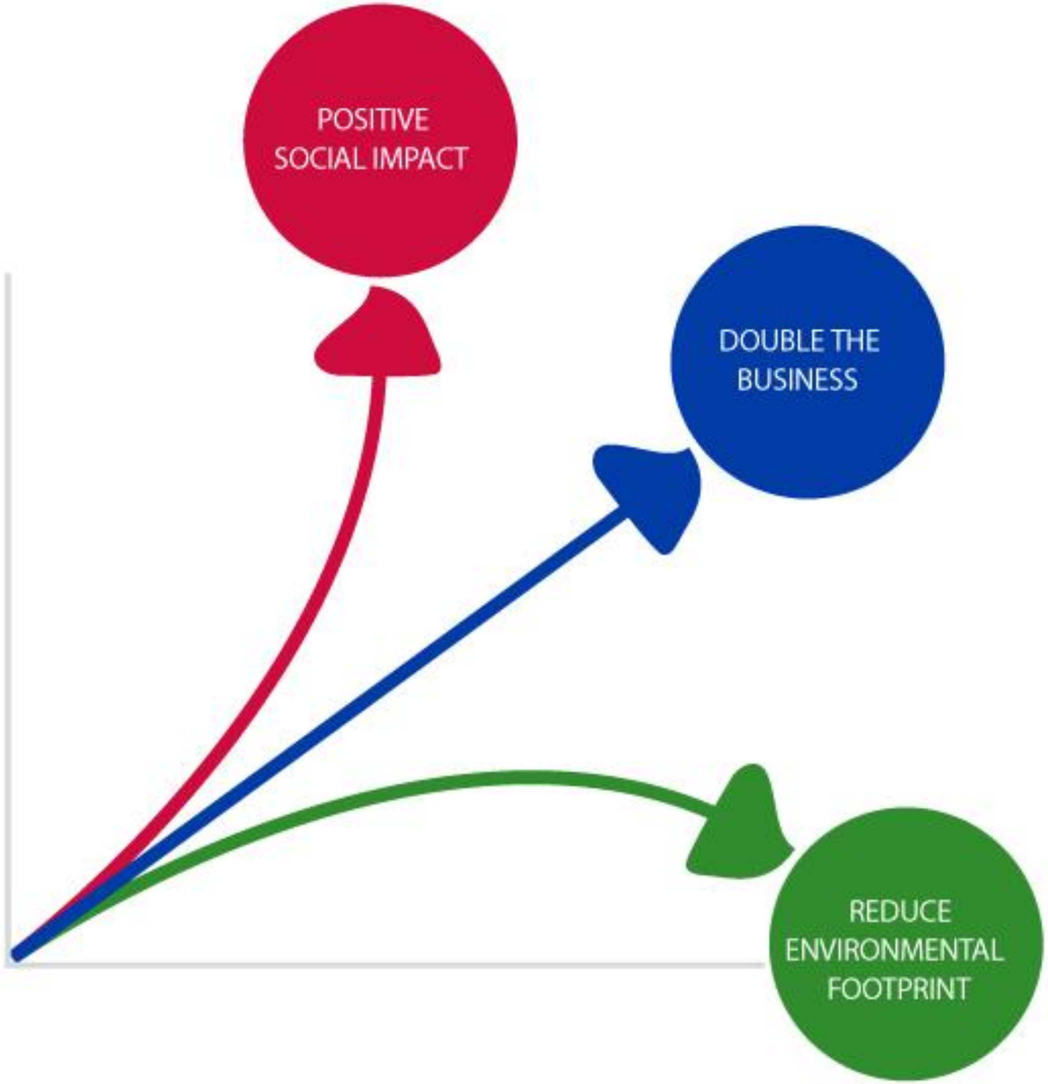
BARRY MURPHY MICROBIOMICS UNILEVER

ABOUT UNILEVER

Unilever is one of the world's leading suppliers of fast-moving consumer goods.

Our products are sold in over 190 countries and used by 2 billion consumers every day.

OUR COMPASS STRATEGY



Our vision is to double the size of the business, whilst reducing our environmental footprint and increasing our positive social impact.

The Compass provides a blueprint for success by identifying what we must do to win share and grow volume in every category and country.

OUR €1 BILLION BRANDS

Unilever

14 Unilever brands have a turnover of €1 billion or more

Personal Care
Dove
Rexona
LUX
AXE
sunsilk

Foods
Knorr
HELLMANN'S
FLORA
Rama

Refreshment
Lipton
DRINK POSITIVE
MAGNUM

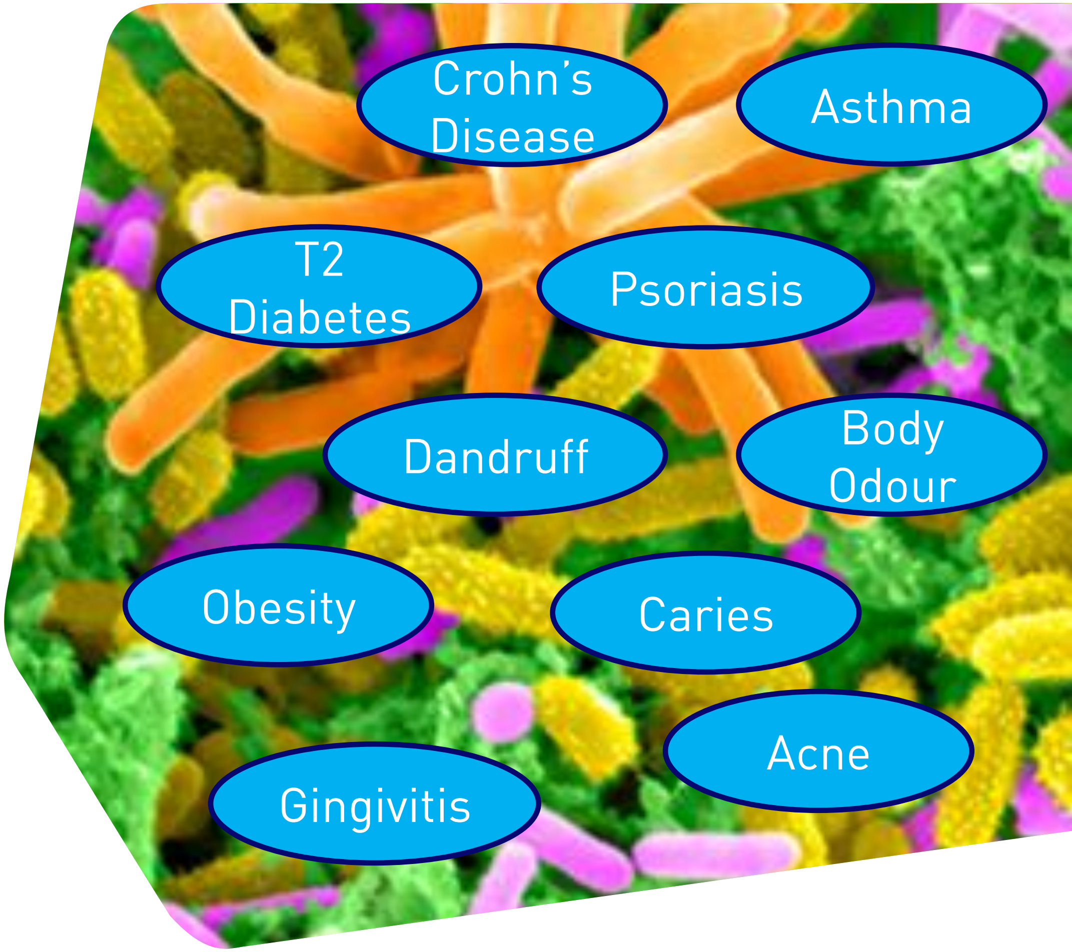
Home Care
dirt is good
Surf

INTEGRATED R&D

- More than 6,000 R&D professionals
- Six key R&D sites delivering groundbreaking technologies: Bangalore (India), Colworth (UK), Port Sunlight (UK) Shanghai (China), Trumbull (US), and Vlaardingen (NL)
- 92 locations around the globe with R&D teams implementing innovations in countries and factories

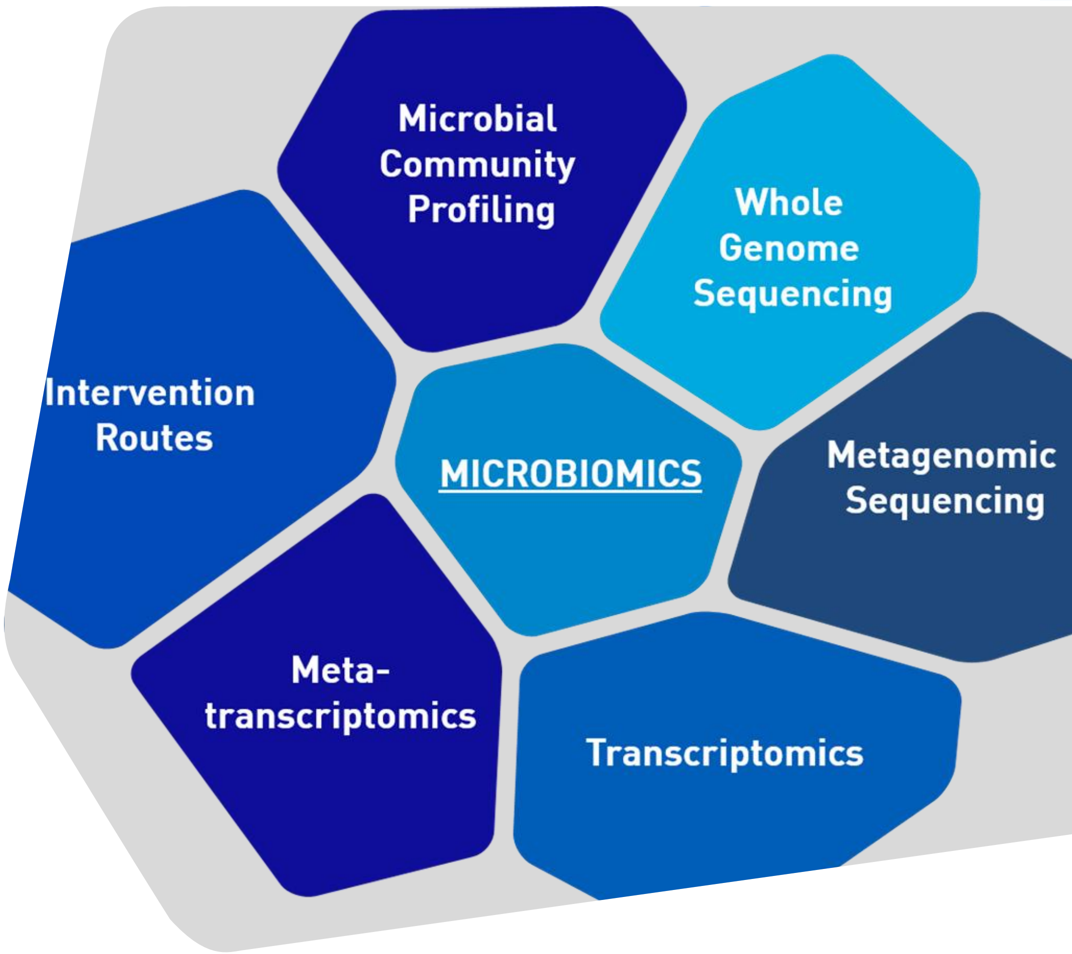
UNDERSTANDING MICROBIAL COMMUNITIES

- Key to a number of Unilever categories.
- Microbial communities implicated in malodour, multiple skin conditions and caries.
- Heightened need to understand the roles of communities and of individual organisms.
- When trying to understand the community it is essential that we do not forget about the host!!!



MICROBIOMICS IN UNILEVER

- A move away from the traditional culture based methods.
- Evolved from 454 to Illumina sequencing.
- Efficient sampling methods for a number of category interests.
- Bioinformatic pipelines in place to process data for taxonomic classification
- While a shift to microbiomics over plates has its advantages there are disadvantages also.



IMPORTANCE OF MICROBIAL COMMUNITIES

- **<u>Deodorants</u>** –Major routes to malodour are VFA's, Odorous steroids and Thioalcohols.
- All are produced by the microbial breakdown of non odorous precursors found in human sweat.
- *Staphylococcus* and *Corynebacterium* implicated in axillary malodour.
- Host genetics important – ABCC11 protein necessary for transport of AA linked thioalcohol precursors.

James *et al.*, 2012; Harker *et al.*, 2014

IMPORTANCE OF MICROBIAL COMMUNITIES

- **Oral Care** - *Streptococcus mutans* strongly linked to caries formation.
- Importance of biofilms in oral care – plaque.
- Production of acids and endotoxins in anaerobic conditions leads to numerous conditions
- *Porphyromonas gingivalis* known to be a "key stone" species in periodontitis.

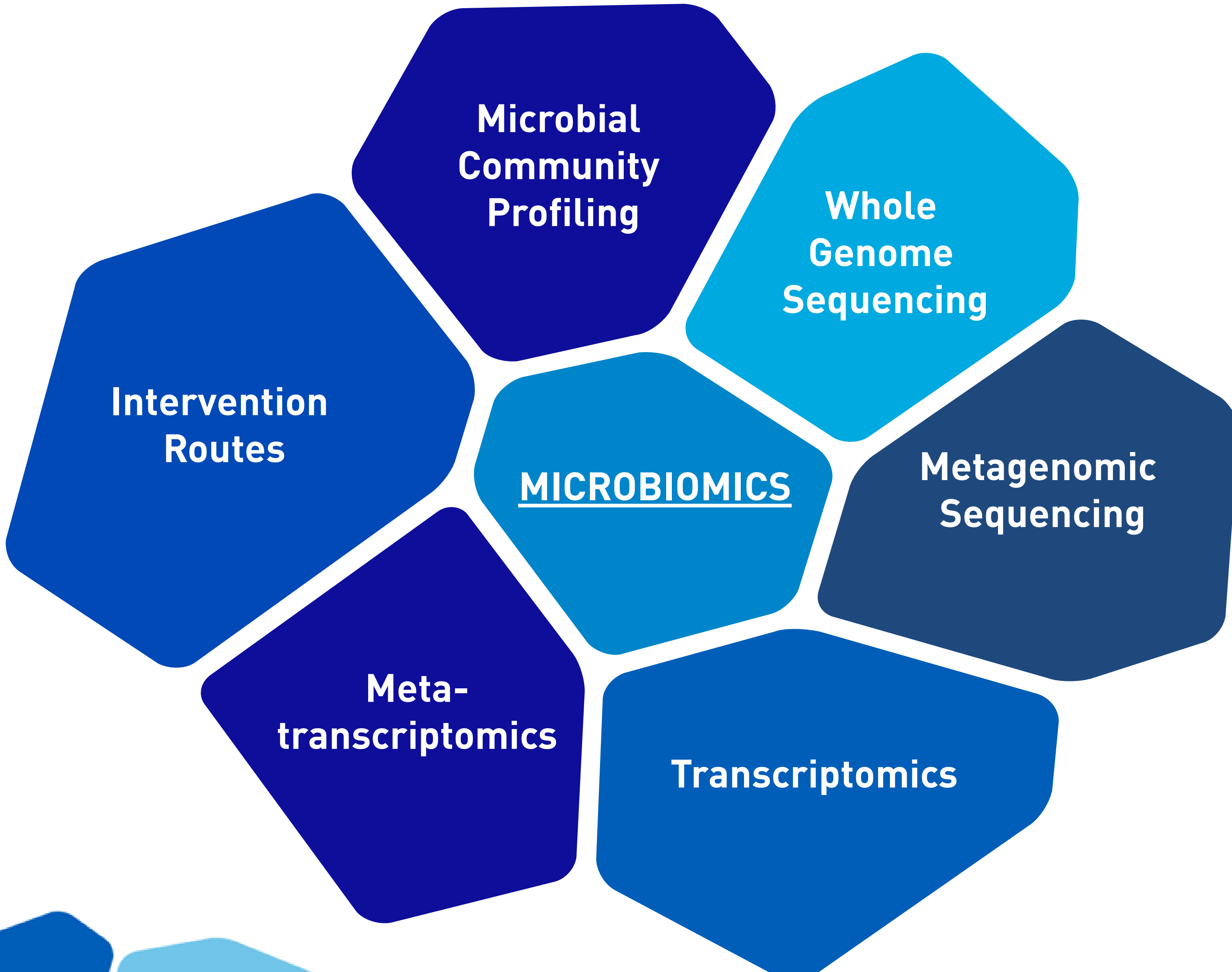
Srinivasan et al., 2013, Adams et al.,2003

IMPORTANCE OF MICROBIAL COMMUNITIES

- **<u>Scalp Care</u>** – Malassezia and *Staphylococcus* spp. implicated in dandruff.
- Outgrowth of particular species associated with dandruff but incomplete understanding.
- Host genetics are possibly important.
- Transcriptomics have been used to elucidate the mode of action of a number of actives.

James *et al.*, 2013; Turner *et al.*, 2012

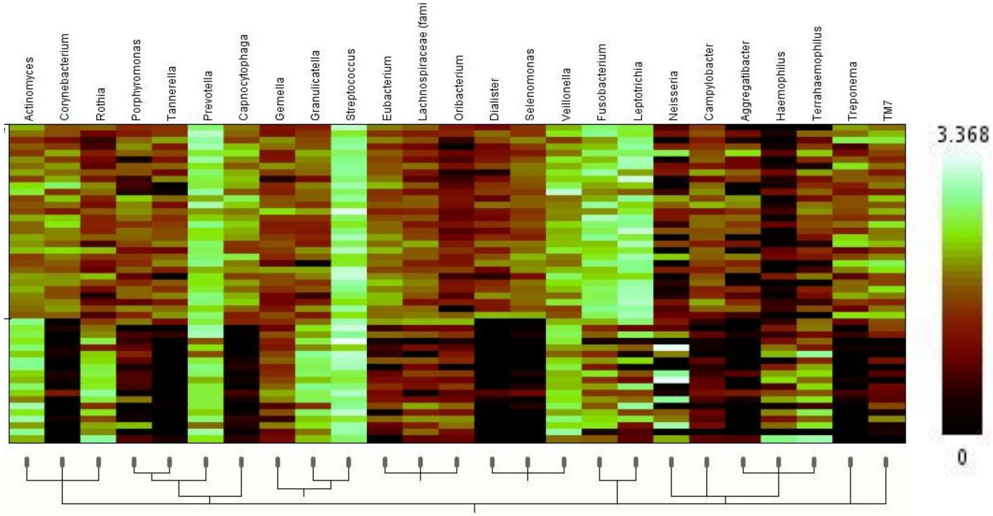
MICROBIOMICS



VISUALISING MICROBIAL COMMUNITIES

Plaque

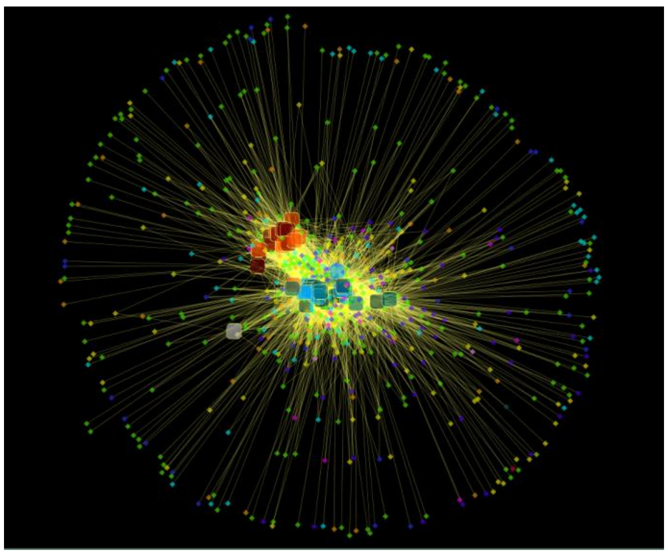
Tongue



Heatmapper

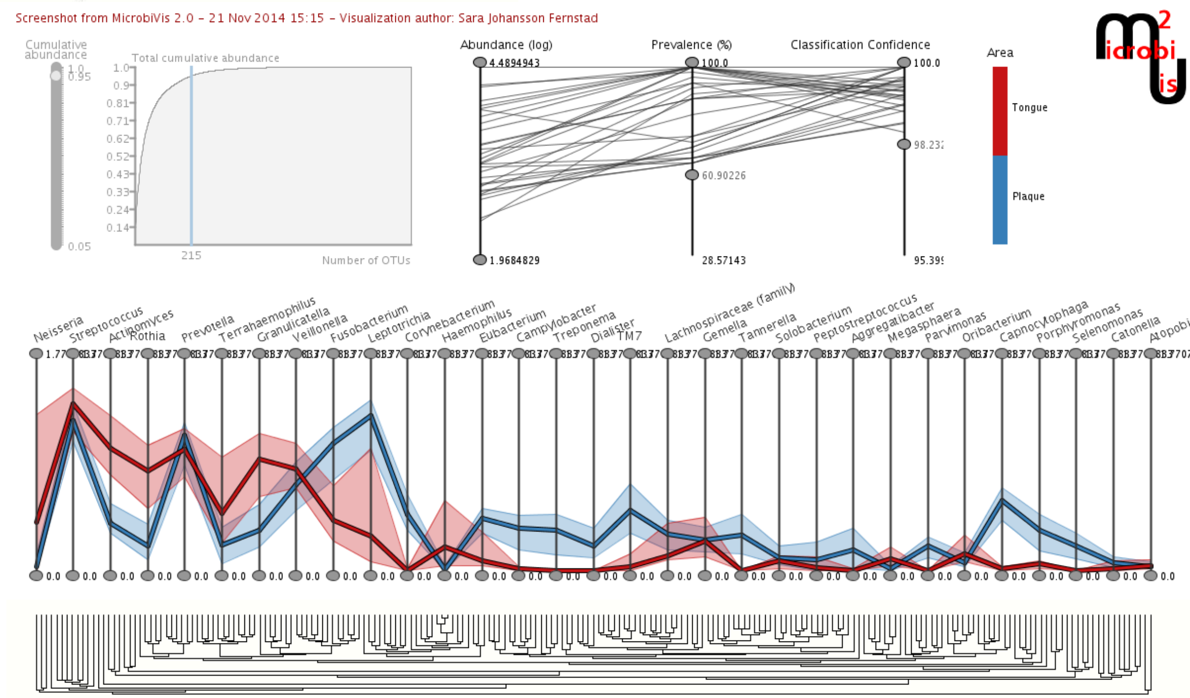
Microbiviz

Cytoscape



Orange/red – tongue

Blue - plaque



FLUX BALANCE ANALYSIS

Compound A → **Compound B** → **Compound C**

Relatively simple analysis when kinetic data is available

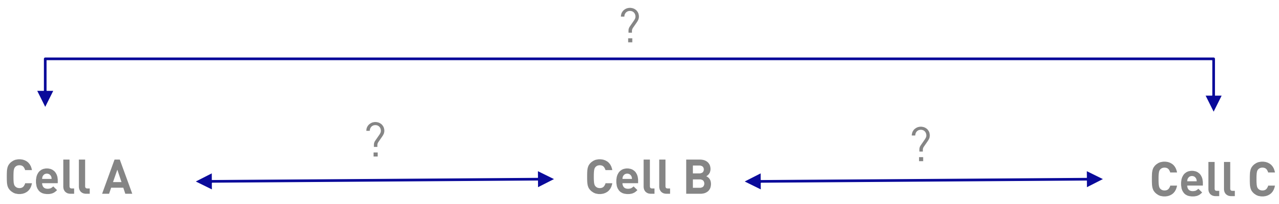
Compound A → **Compound B** → **Compound C**

Compound B → **Compound D**

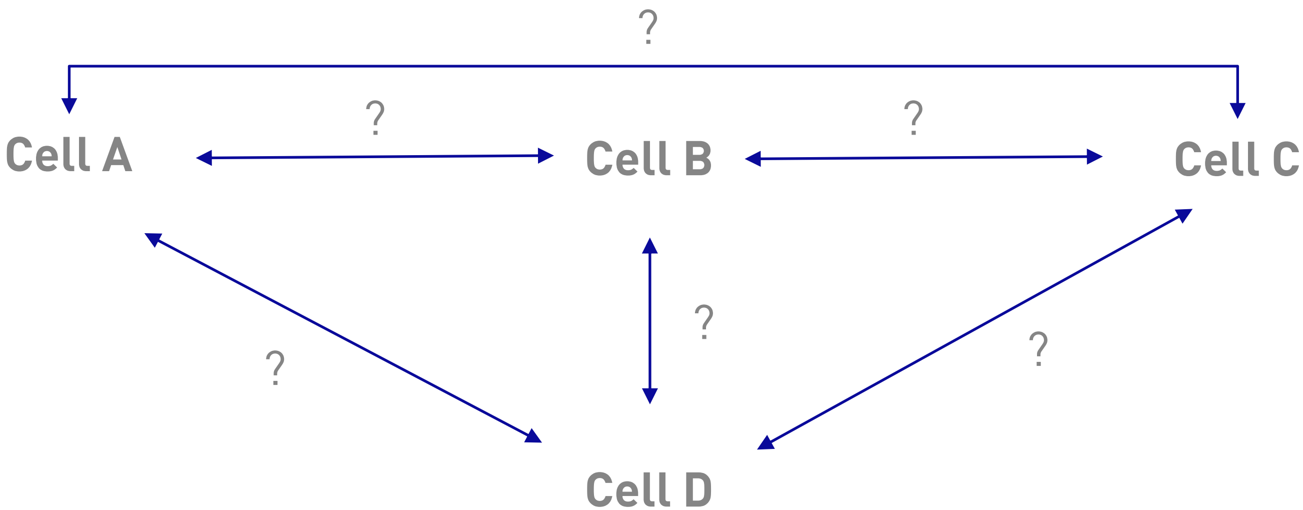
Compound D

Essential in biotechnology in order to improve metabolite production

FLUX BALANCE ANALYSIS



Much more complicated when whole cells are used in this context

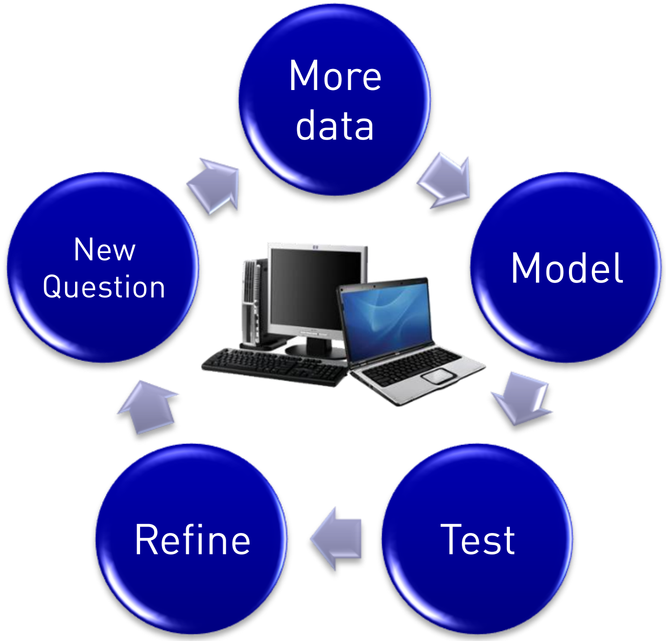


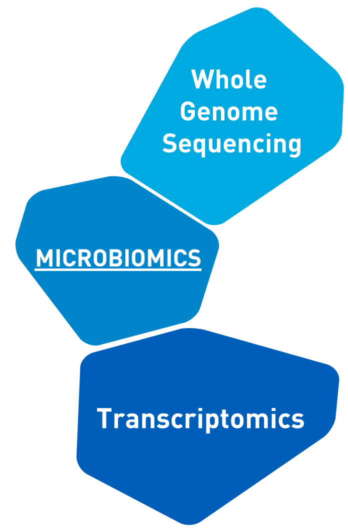
How can we model these relationships? How much data do we need?

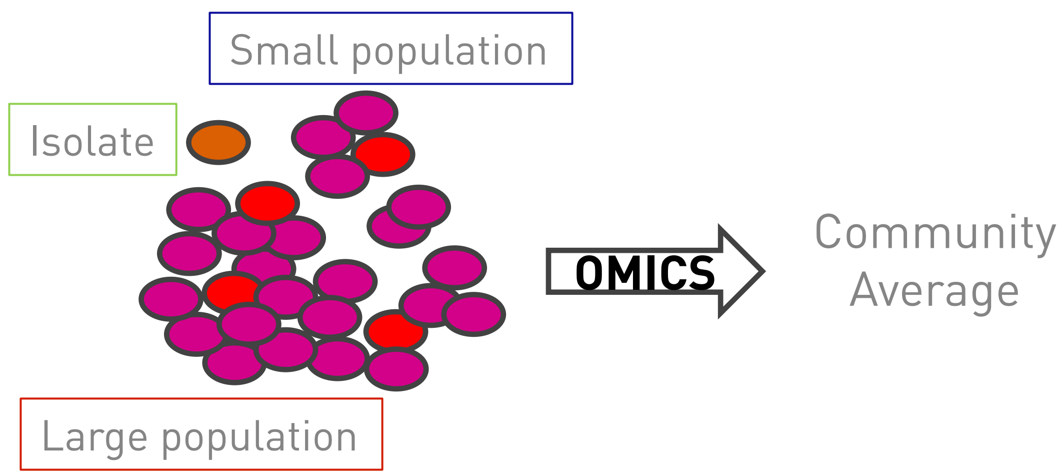
FLUX BALANCE ANALYSIS IN "PURE" CULTURE

- Using RNA seq data to determine expression profiles in response to actives.
- Possible to use data to develop *in silico* constraint based models for further analysis.

- Numerous assumptions being made including that the population is homogenous.
- Also does not represent the true state of the organism *in vivo* with regard to community interactions.

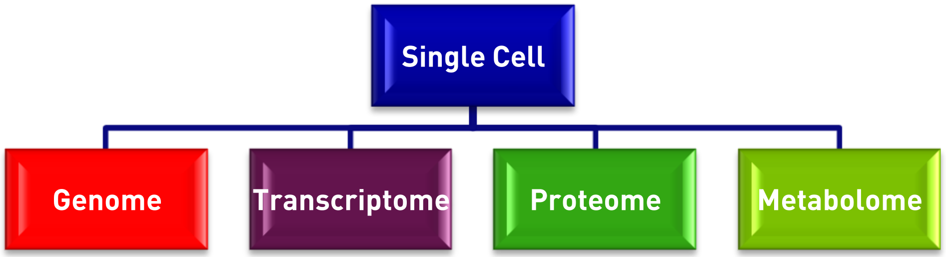


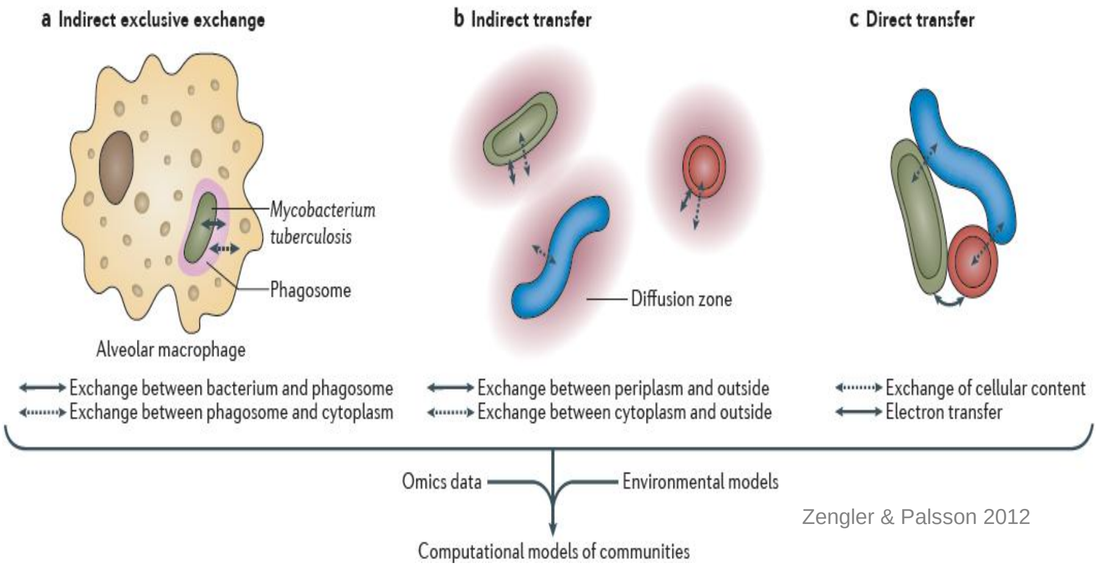




SYSTEMS BIOLOGY: BOTTOM UP APPROACHES

- Cultivation approaches will result in dominant/less fastidious taxa being analysed. Must go beyond barcode analysis.
- Does not take into account interactions between community members (+ve/-ve/neutral) and host/environment.
- Genome Scale Metabolic Reconstruction
- Will this form of analysis even be needed in the future. What is there v's what are they doing?

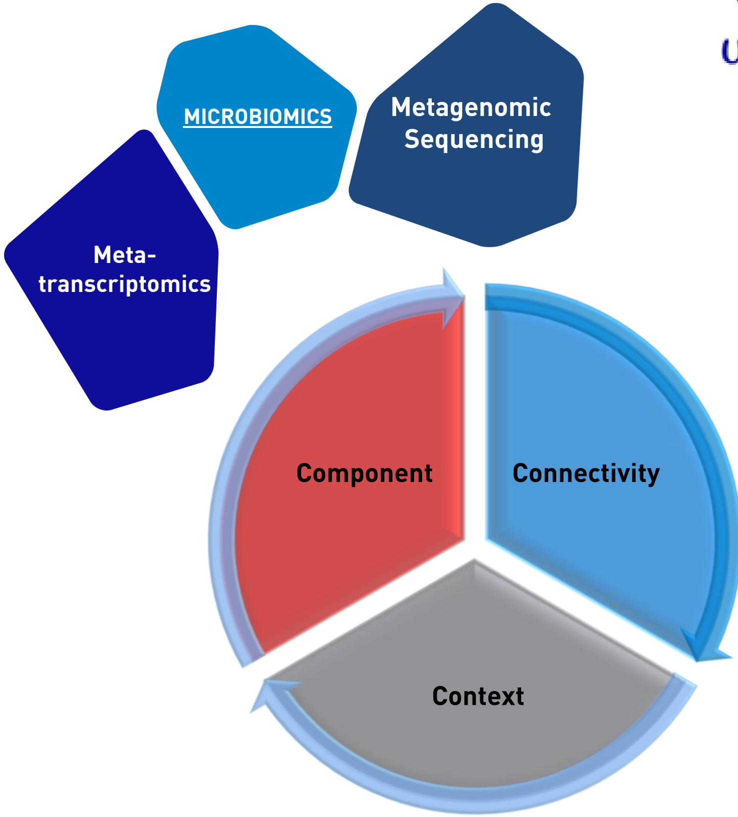




Zengler & Palsson 2012

SYSTEMS BIOLOGY: TOP DOWN APPROACHES

- Can target whole community but lack of resolution.
- May allow the study of community interactions without knowing key members.
- Requires the integration of multiple datasets across species.
- Genomics leading the way but other techniques need to evolve further.
- Better datasets and databases are needed, Kyrpides et al., 2014.



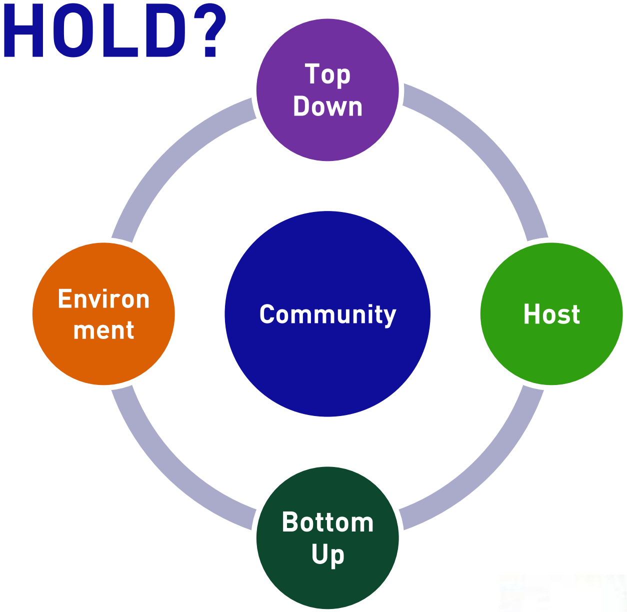
Excellent
- Genomics
- Transcriptomics
- Epigenomics

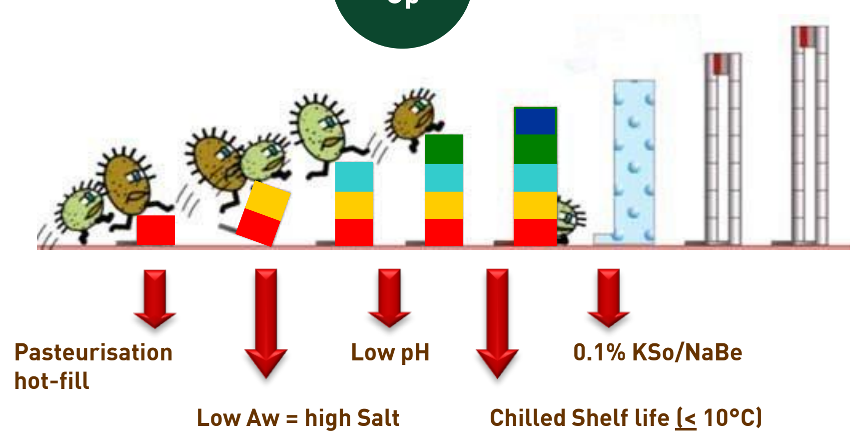
Developing
- Metabolomics
- Lipidomics

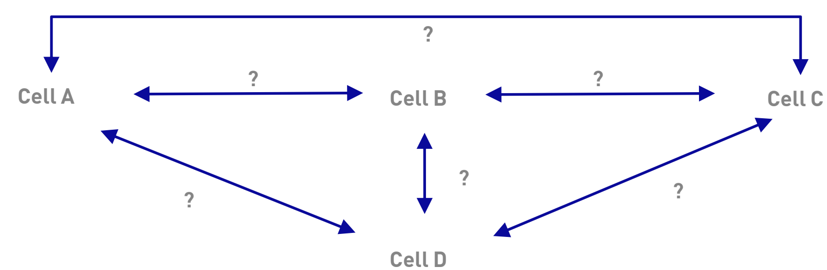
Basic
- Proteomics

WHAT WILL THE FUTURE HOLD?

- Multi-integration strategies (Weight)
- Predictive modelling can be used to evaluate intervention routes, quicker/cheaper/safer.
- Can predictive models be used to determine the effect of broad spectrum antimicrobials / hurdles.
- Community model where affect of removing a particular species is revealed. How will the remaining members adapt to fill the niche?







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