waag society

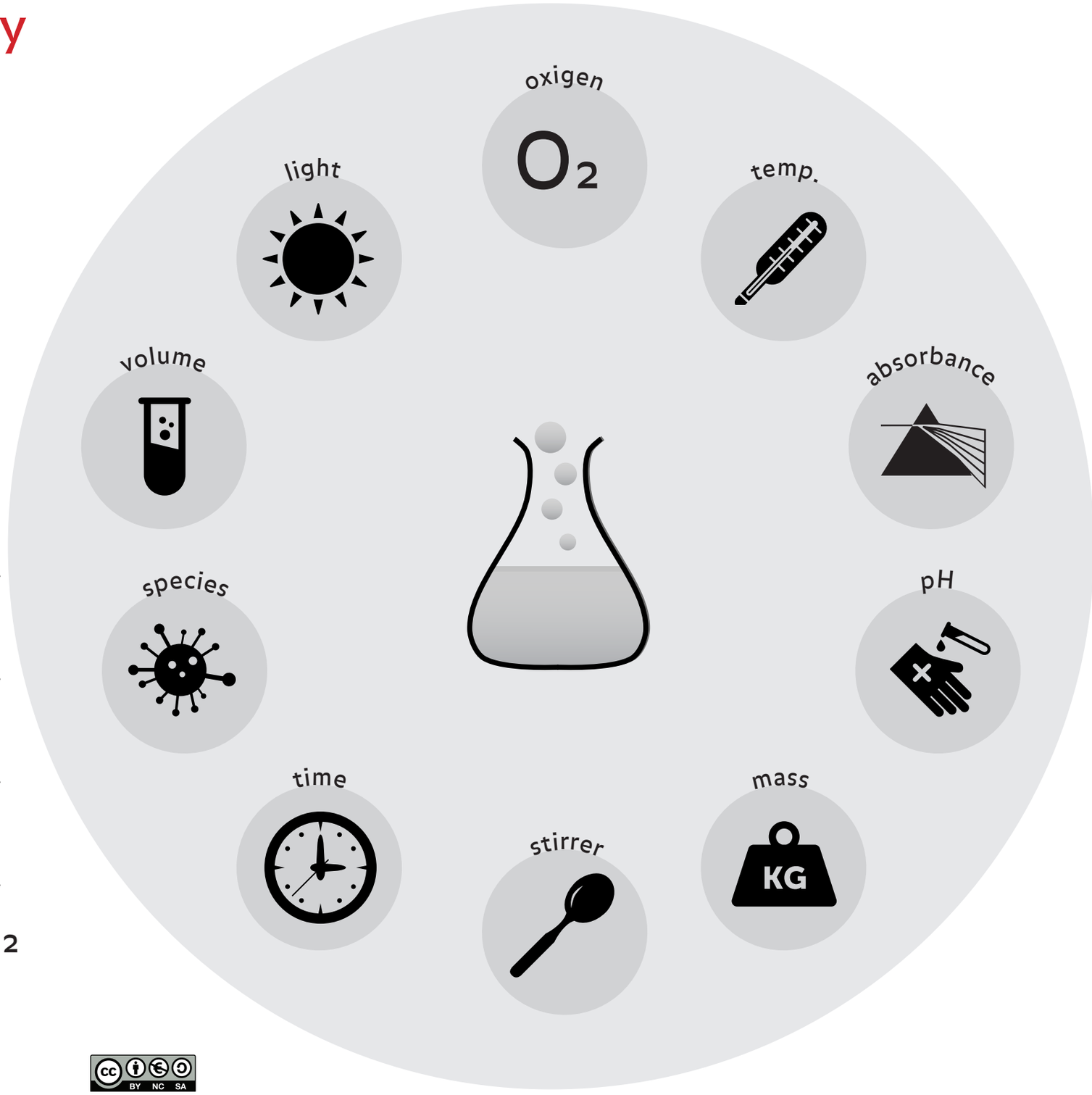
institute for art, science and technology

picture by Gerrit Niezen

BioHack Academy
Growth & Production

BioFactory
canvas

open wetlab
waag society



input

C

N

P

O_2

S

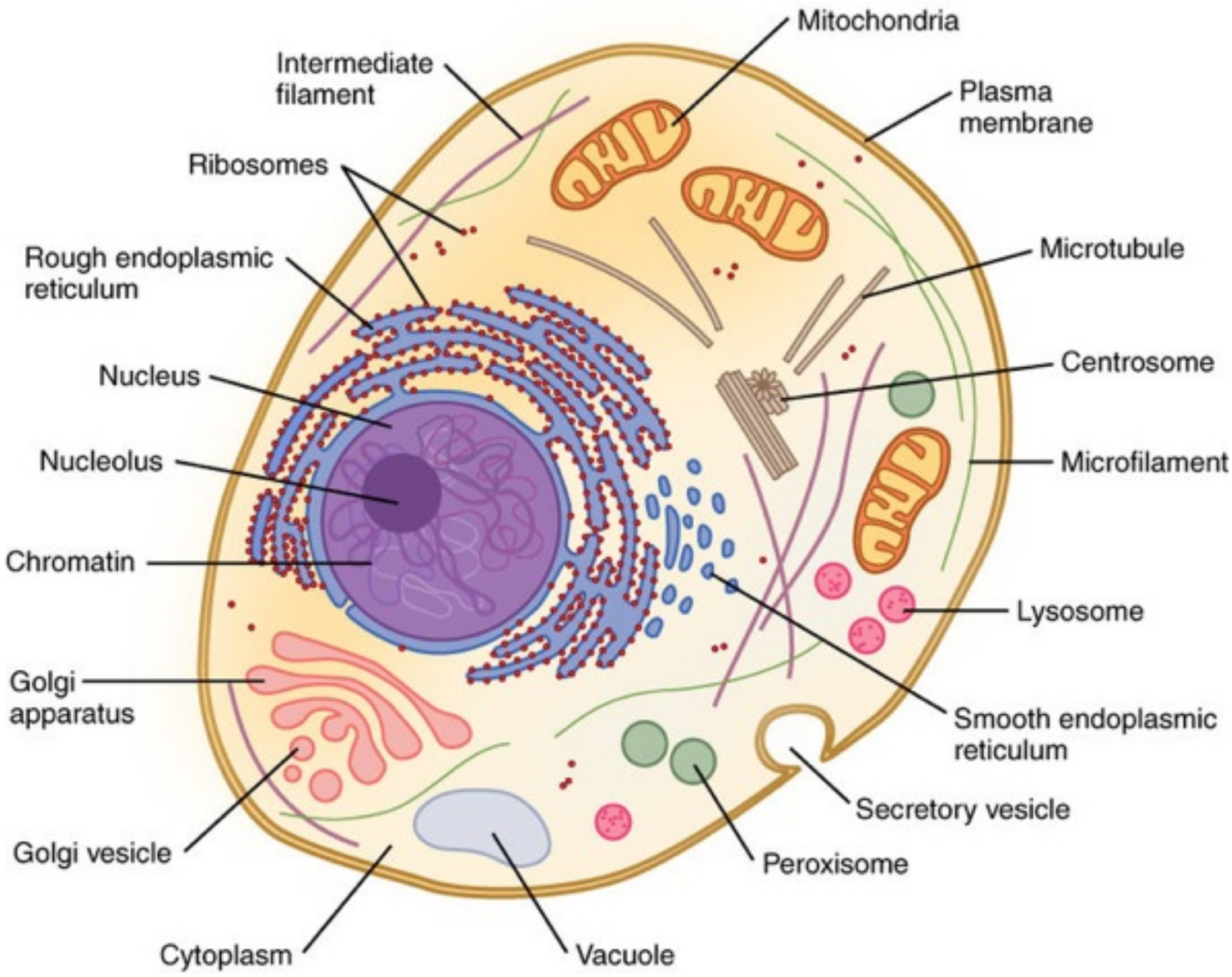
observations

day #	
day #	
day #	
day #	
day #	

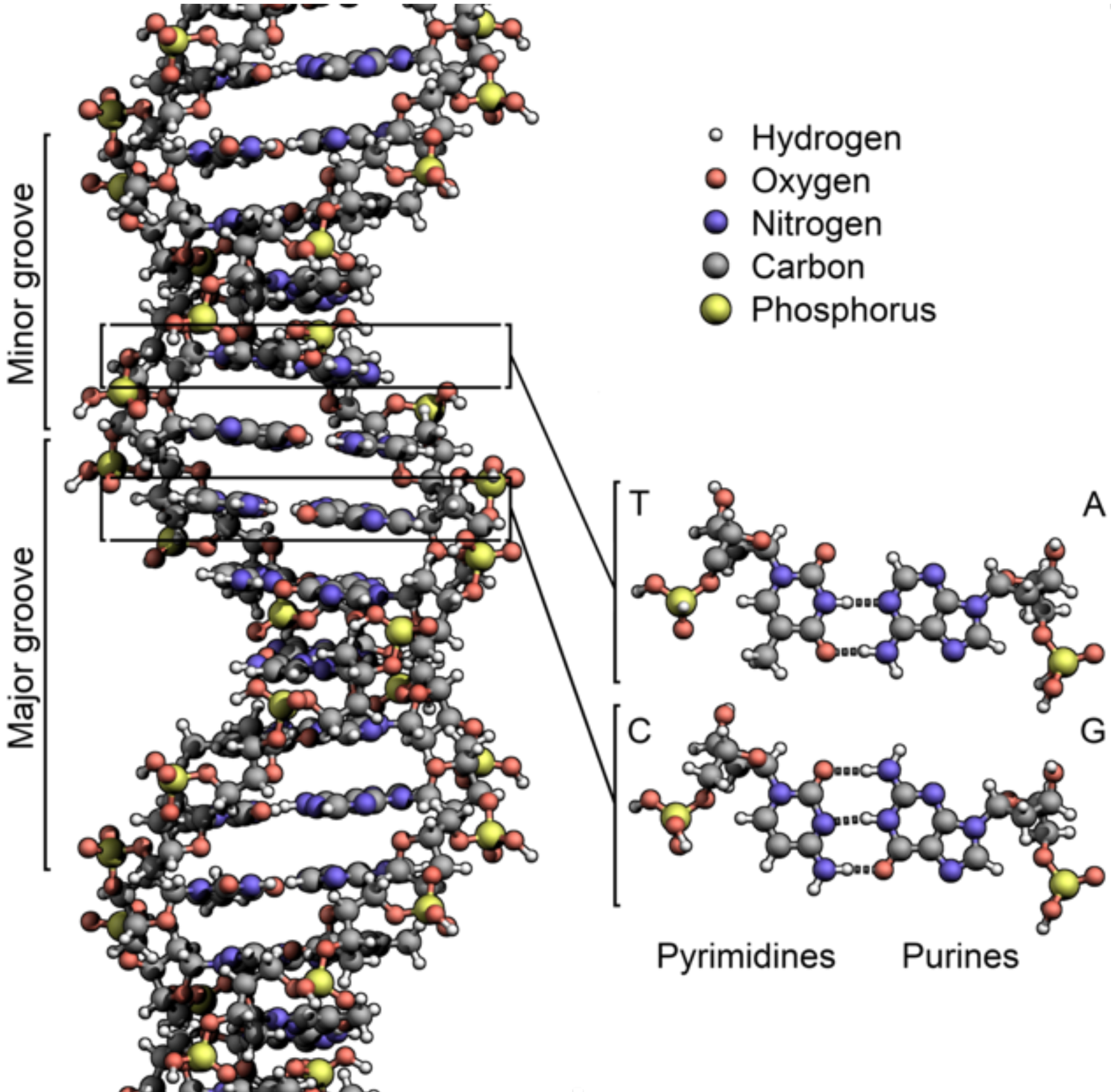
material

What's a cell made of:

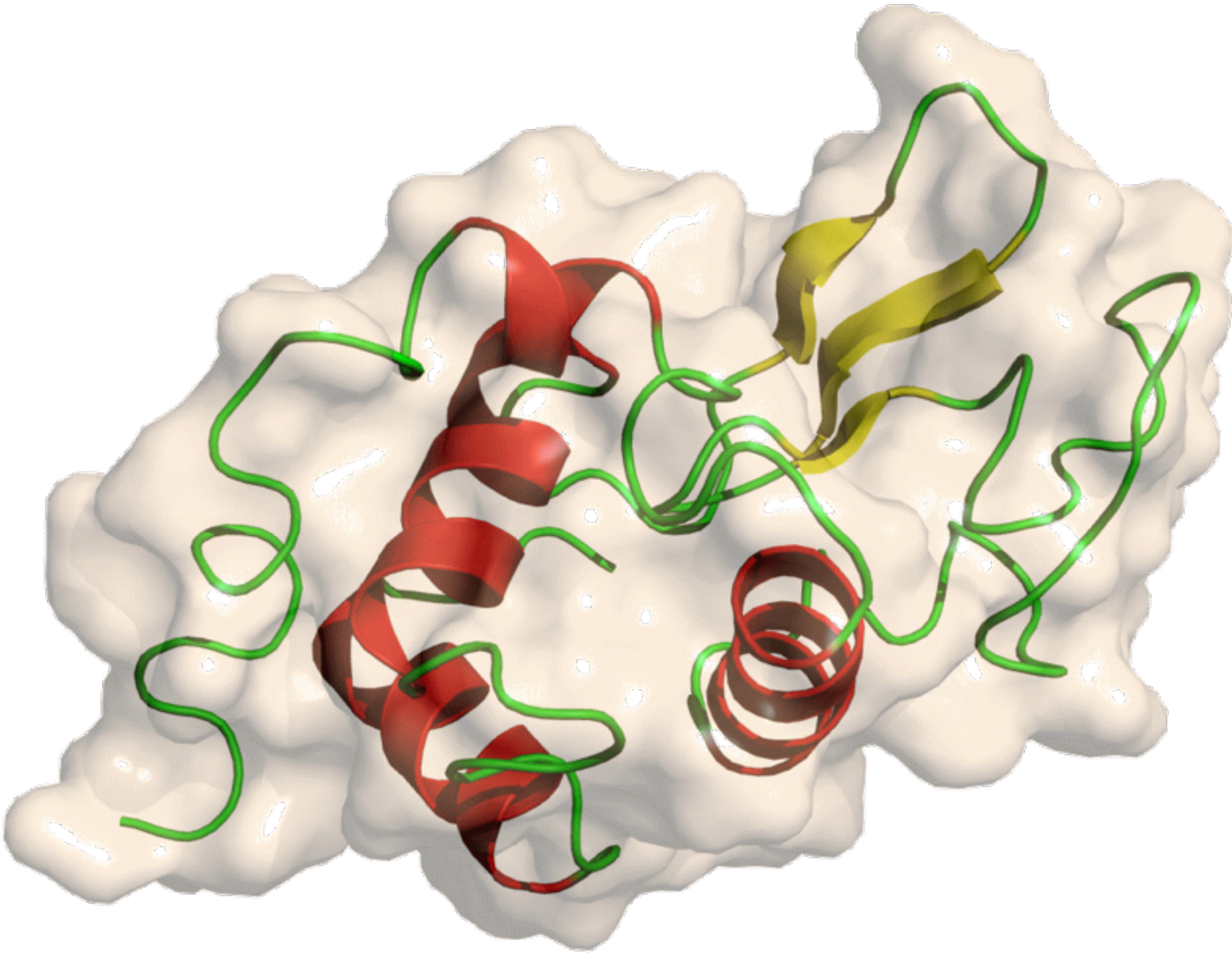
- Lipids
- Proteins
- DNA
- RNA
- Metabolites
- Ions



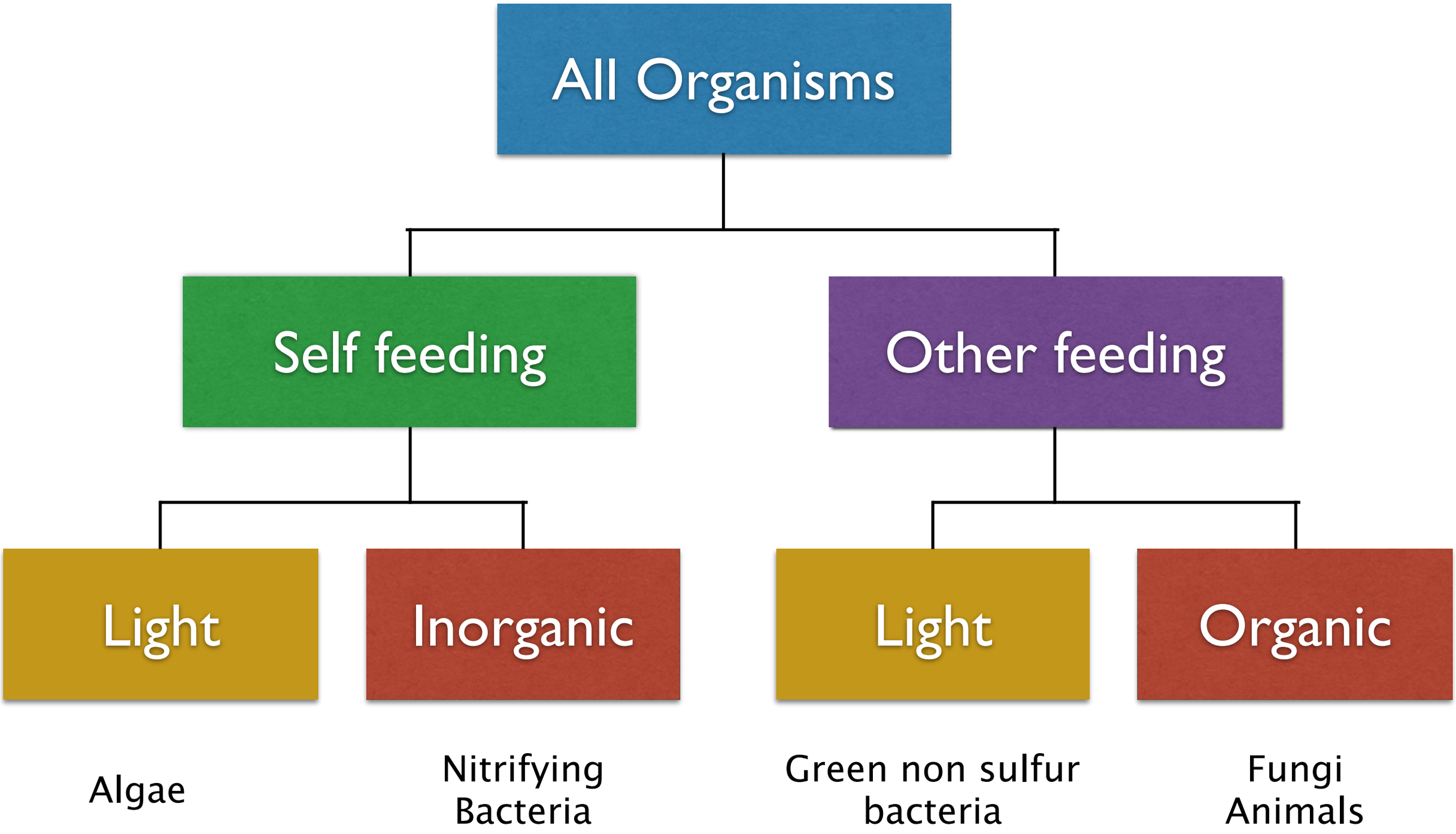
DNA Molecule



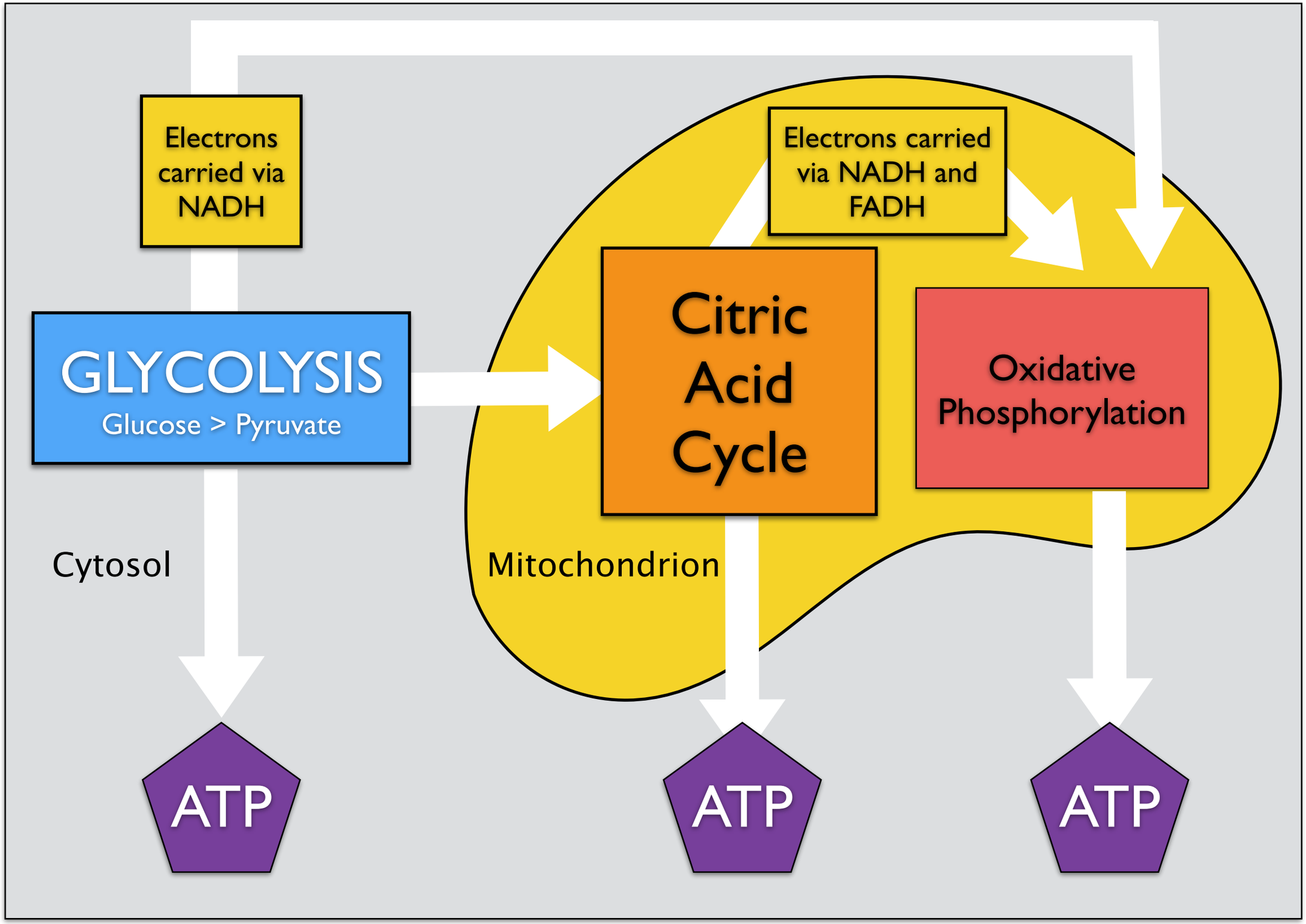
Lysozyme



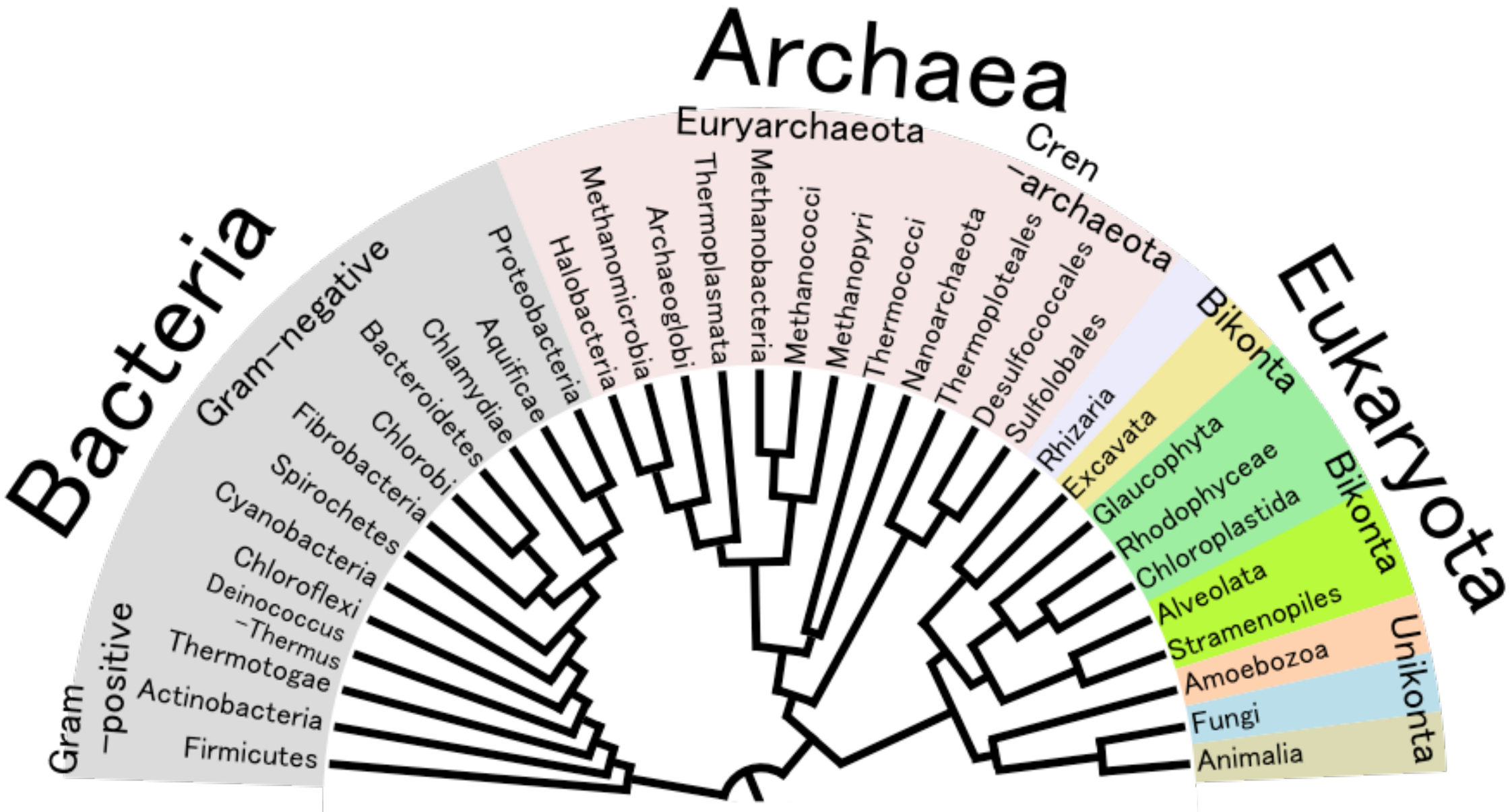
Diversity in Metabolism



Respiration

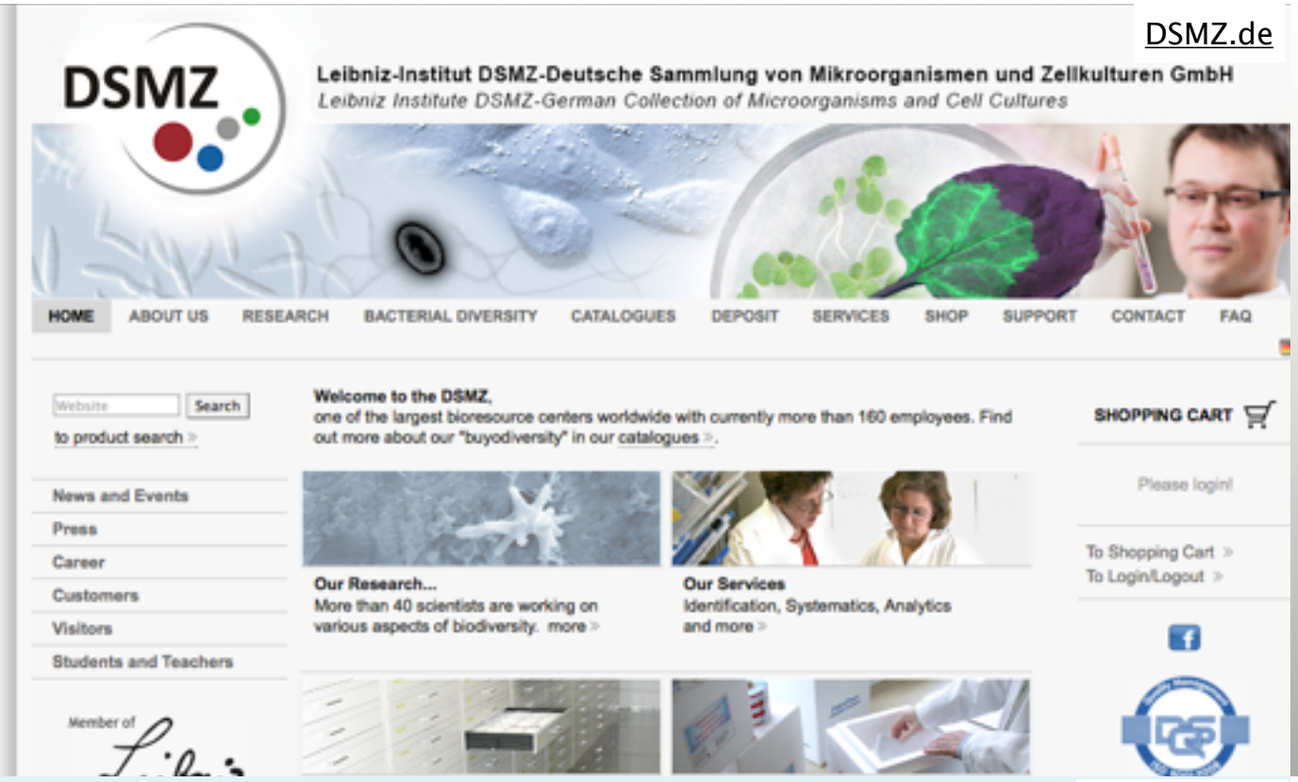


Species vs Strains

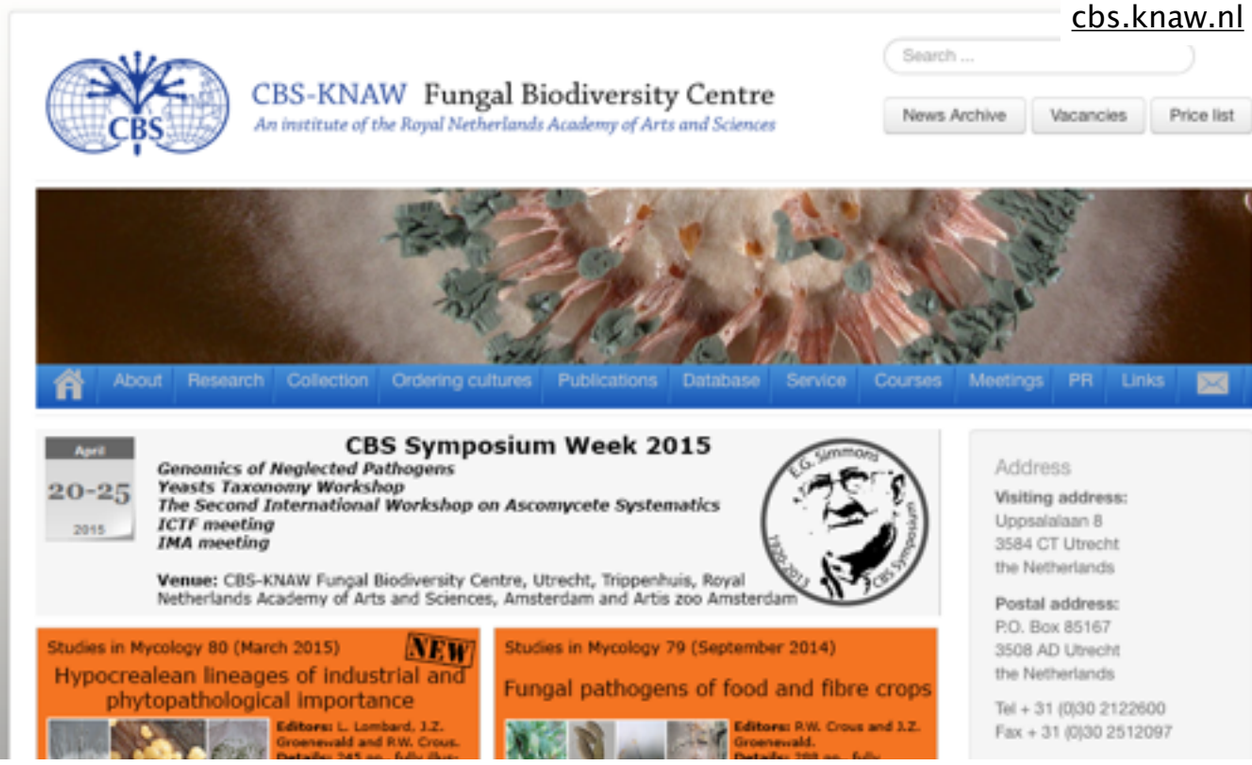


Culture collections

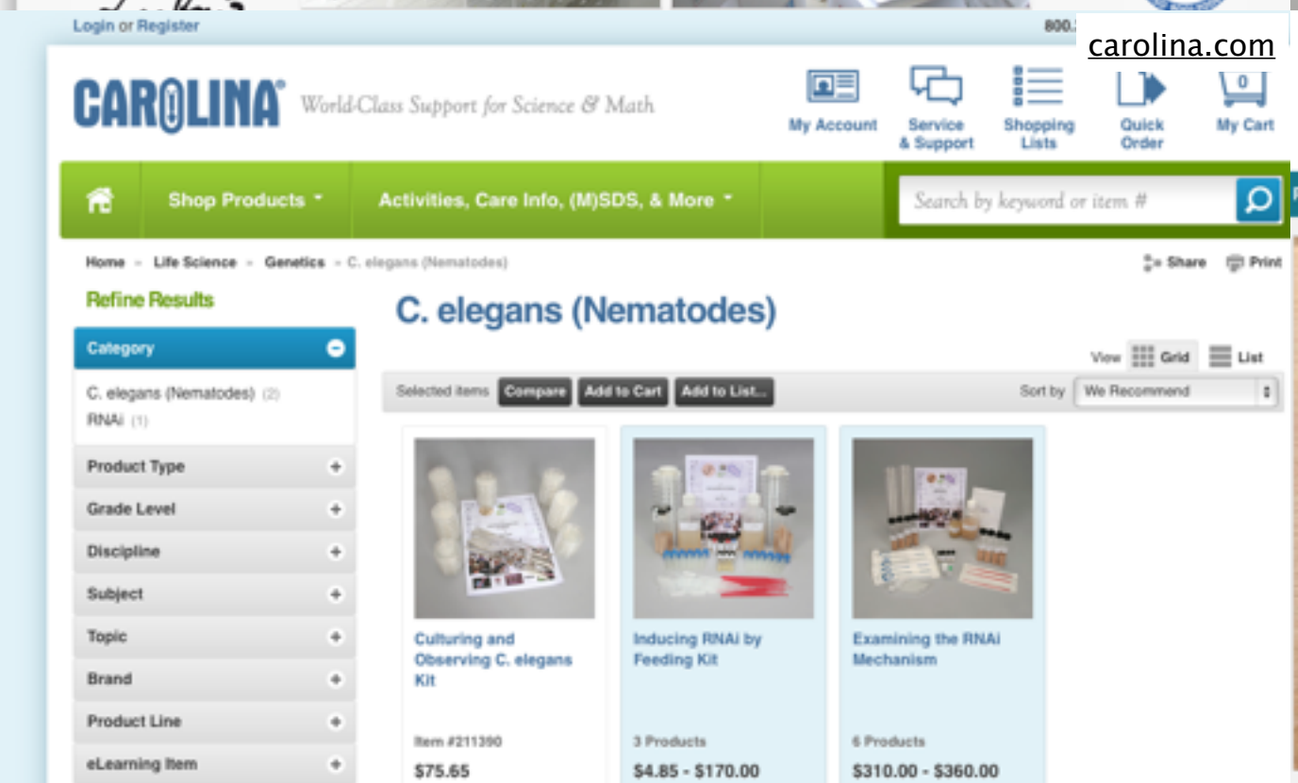
DSMZ.de



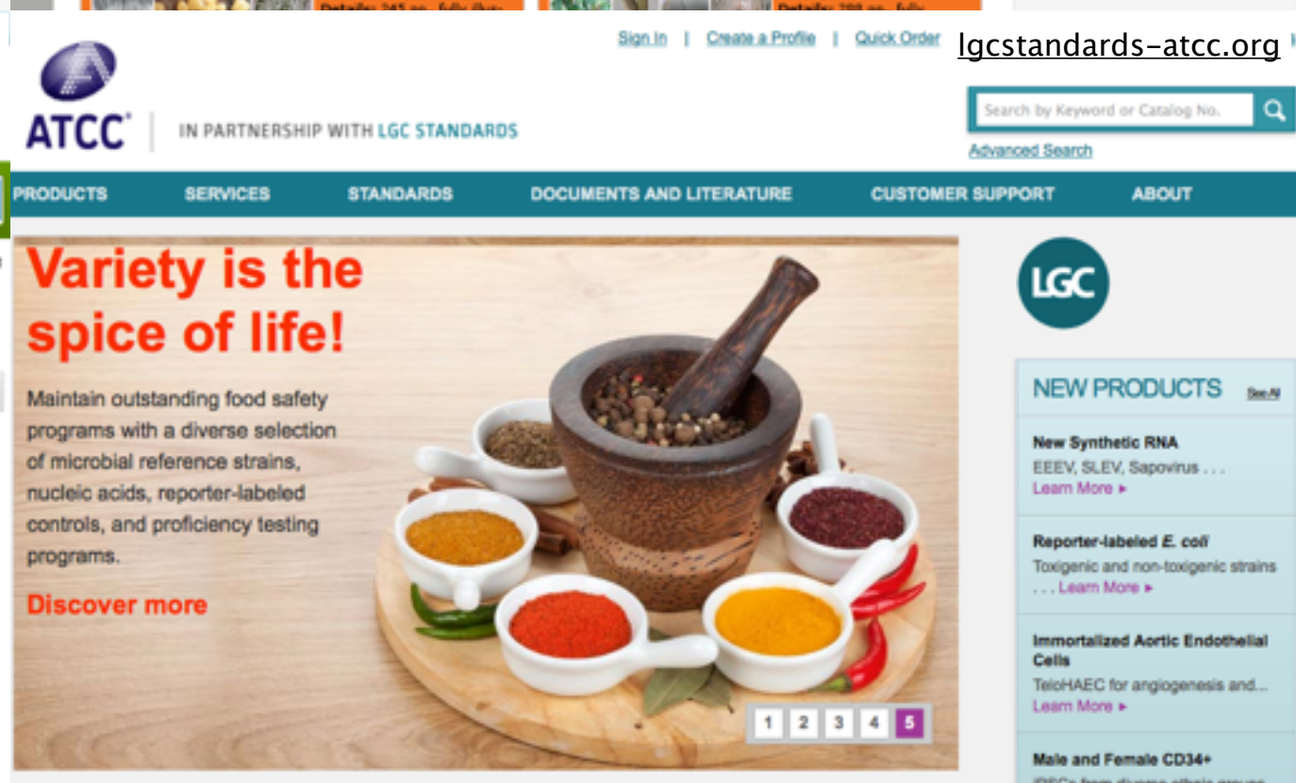
cbs.knaw.nl



carolina.com

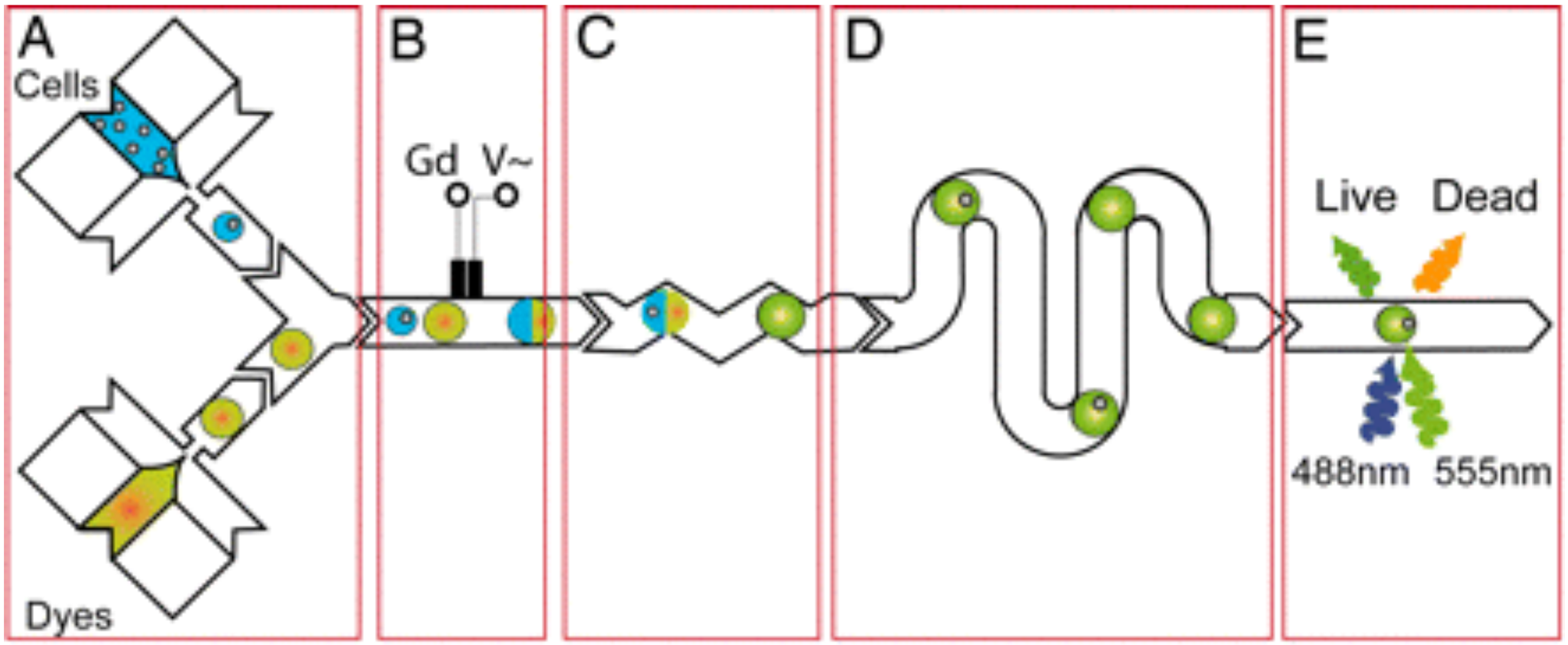


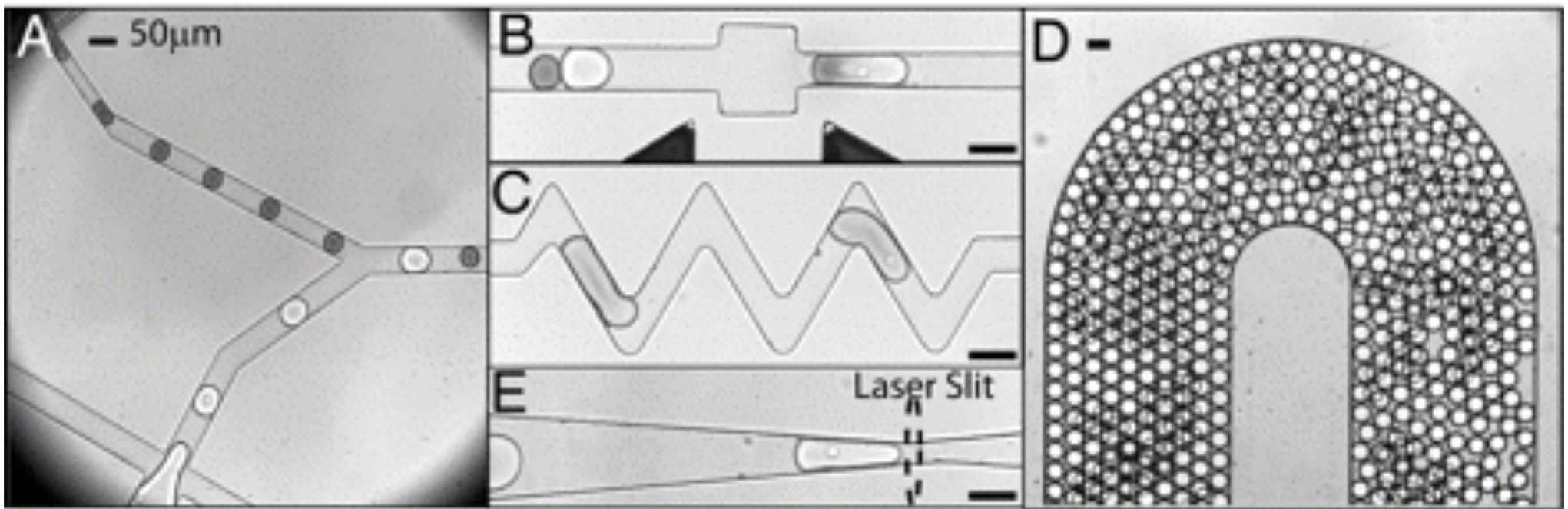
lgcstandards-atcc.org



High Throughput Screening

Eric Brouzes et al. PNAS 2009;106:14195-14200



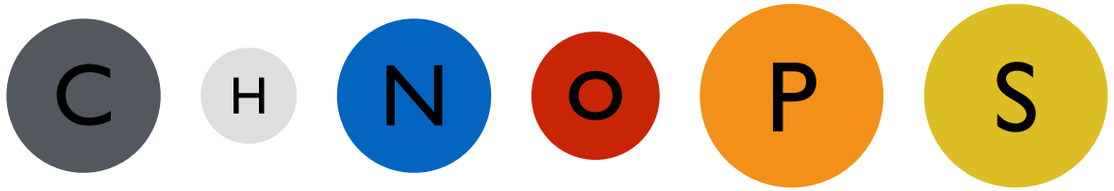


Electrowetting

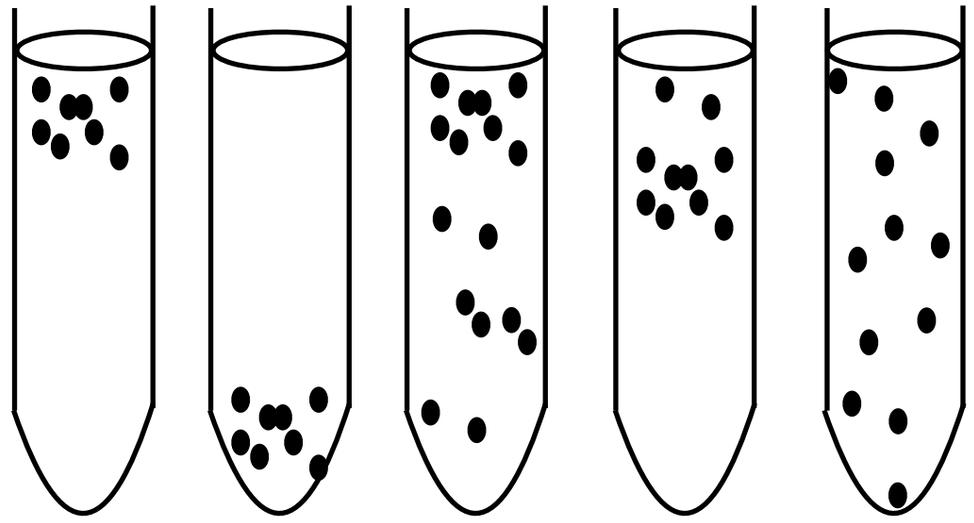
https://www.youtube.com/watch?v=DJgvBoygmgk

Diversity due to growth conditions

Nutrients



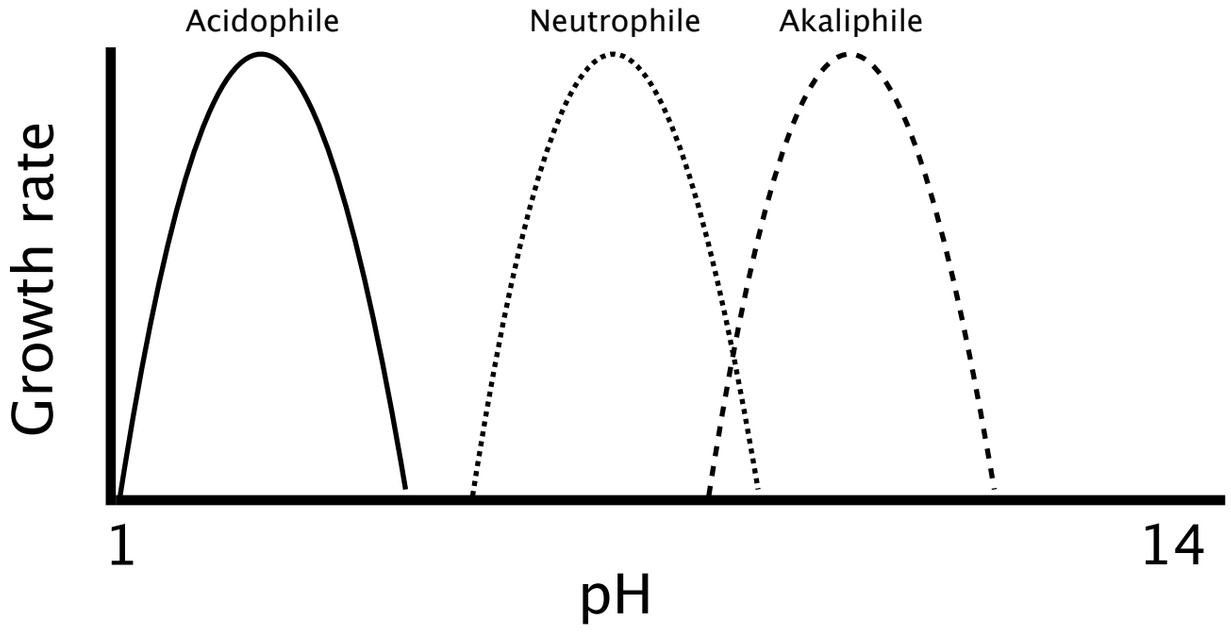
Atmosphere



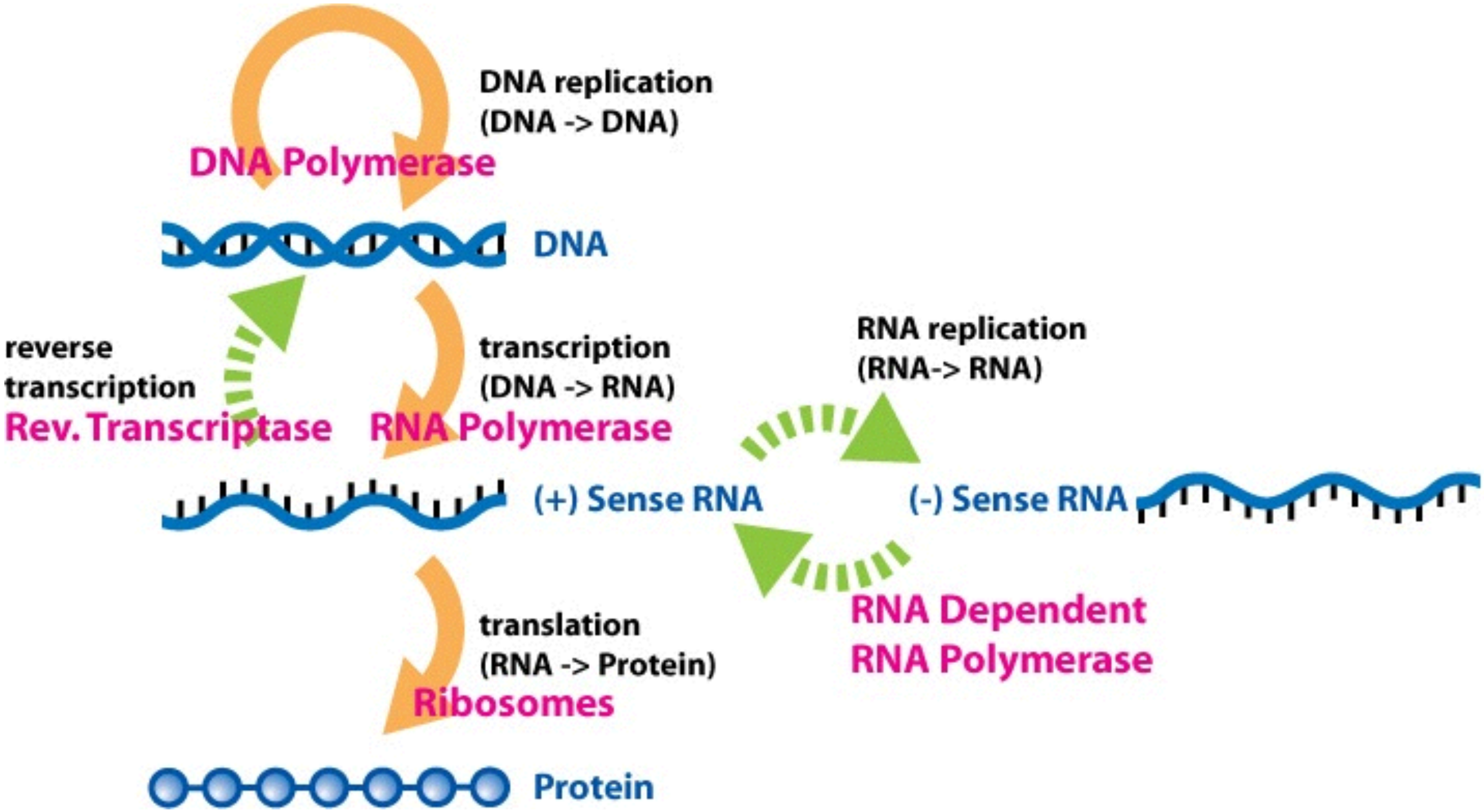
Temperature

Pixabay - CC0

pH



Influencing gene expression



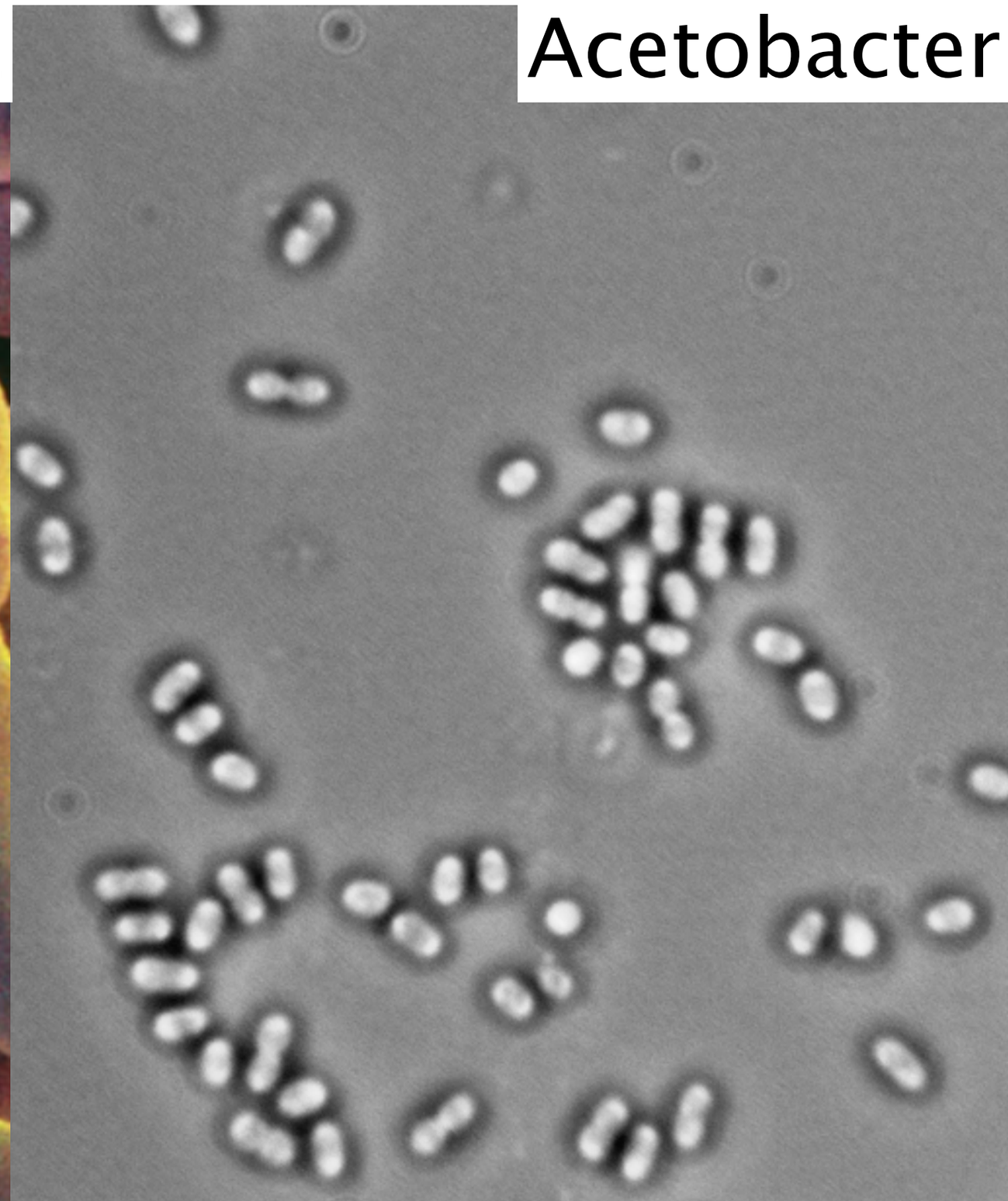
What we are looking for

- High yield
  - Conversion of substrate into product
- Fast growing
- Low amount of (toxic) by-products
- Easy to purify
- Robust cells

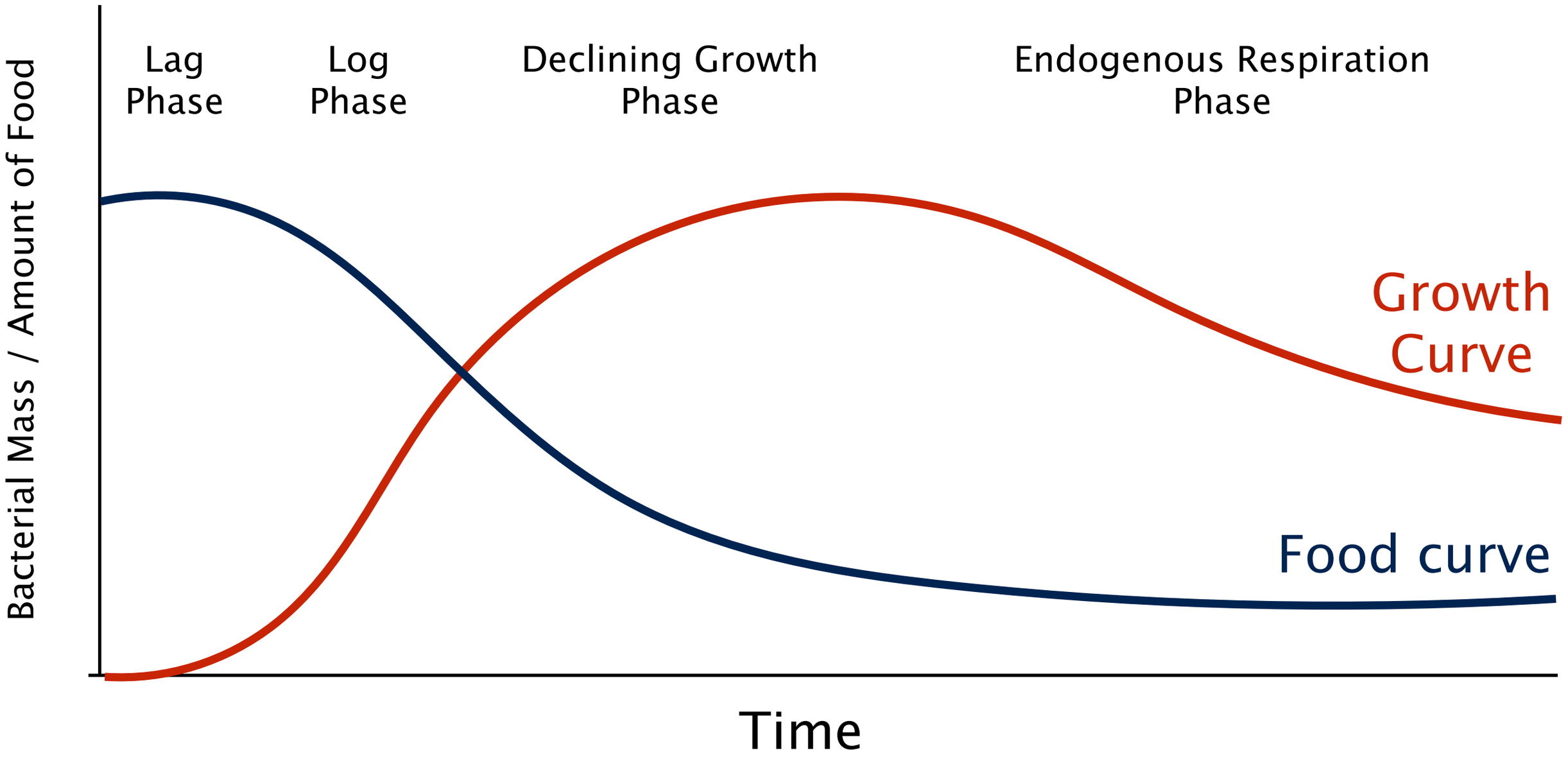
Natural talents

Yeast

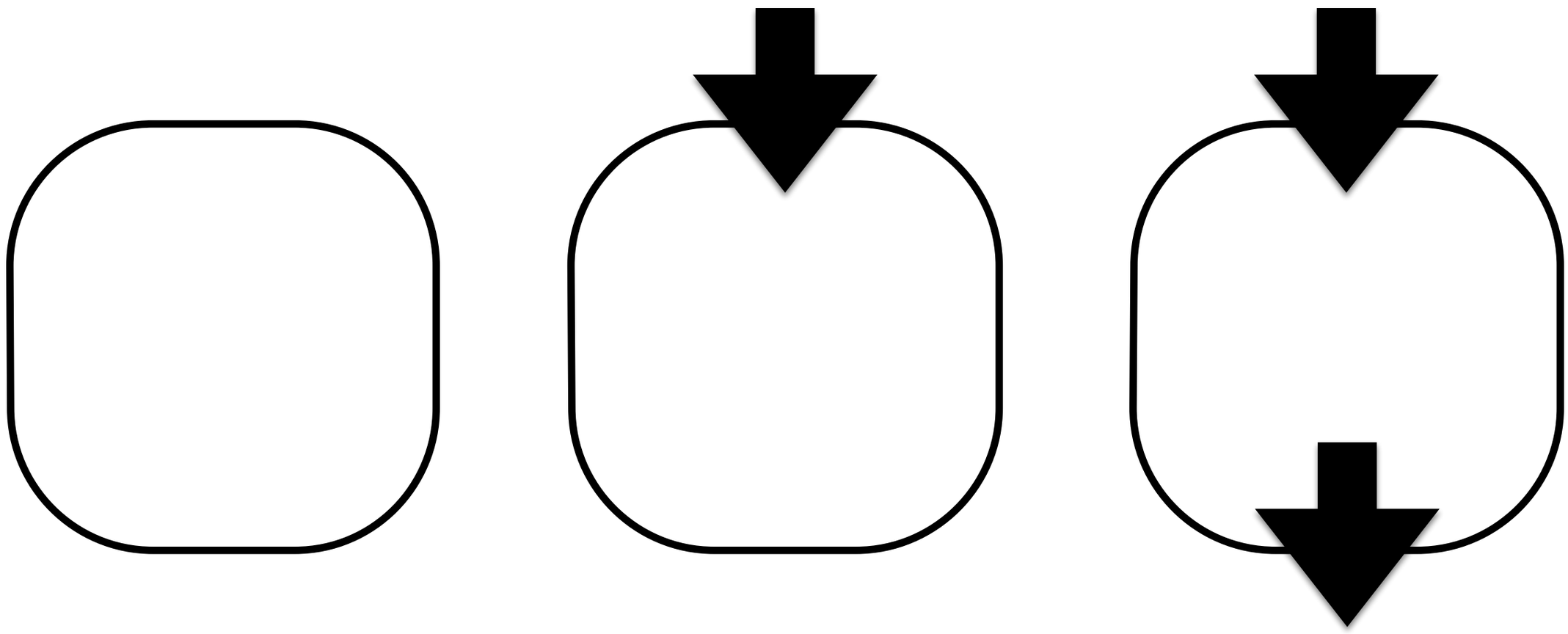
Acetobacter



Bacterial growth curve – Batch



Growth strategies



Batch

Fed Batch

Chemostat

Advantages of chemostat

- Measure specific growth speed
- Investigate effect of medium
- Measure & control environmental parameters

Large scale chemostats

Fusarium graminareum

Saccharomyces cerevisiae

Single use bioreactors

- Instability
- Contamination risk
- Flexibility
- Down stream processing is discontinuous

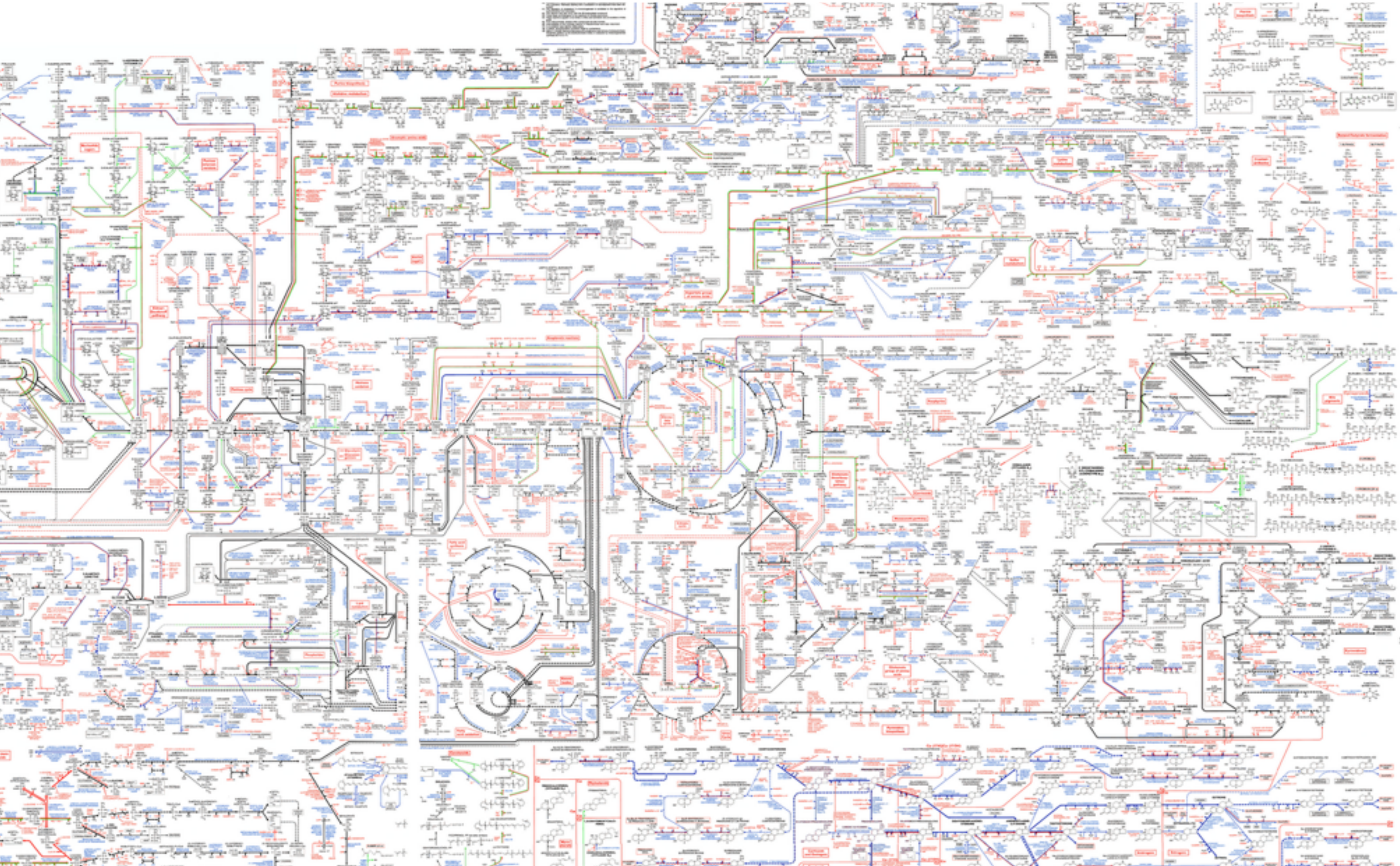
100 m3 reactor

- Yeast production
- Yield = product / substrate

- Fermentation: 2 ATP per sugar
- Respiration: 16 ATP per sugar

- Even at full aeration risk of low yield: Respirofermentive metabolism

Metabolic engineering



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Growth Stoichiometry

Divide by Molecular Weight

Multiply 6.022×10^{23}

Grams

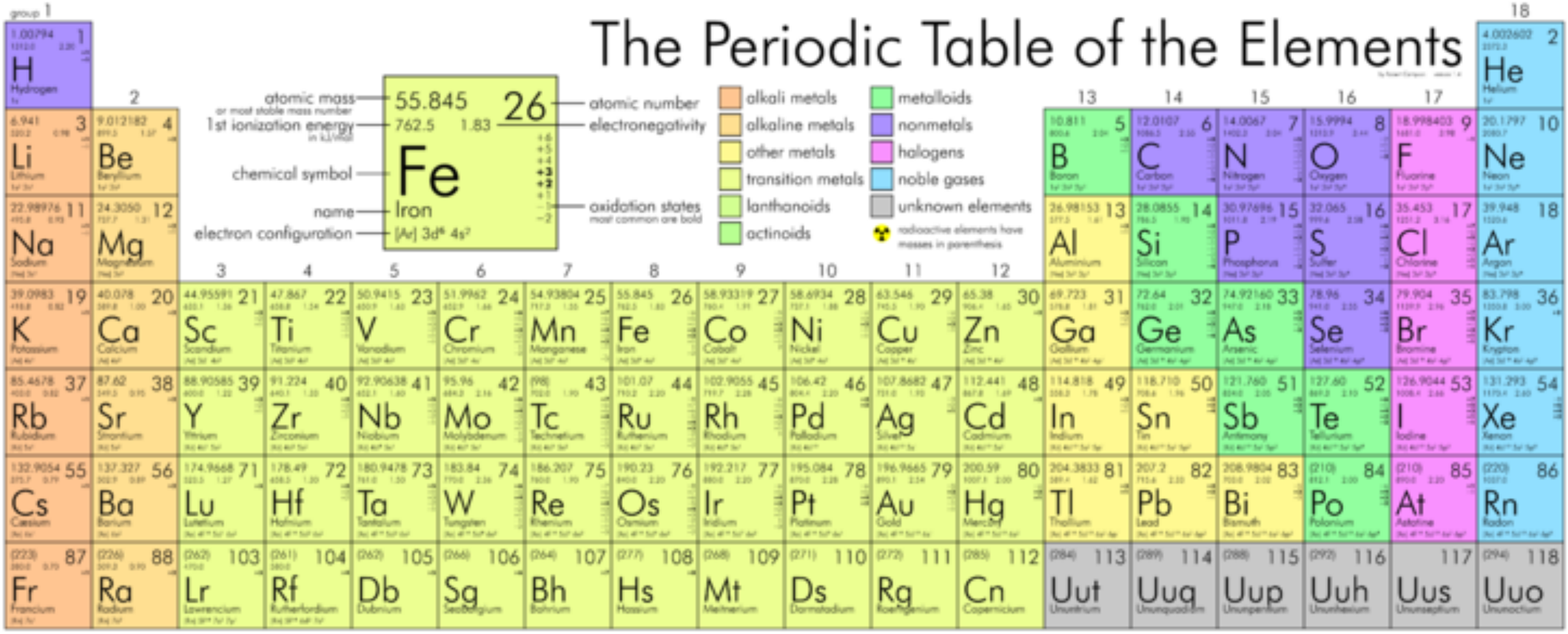
Moles

Number of molecules

Multiply Molecular Weight

Divide by 6.022×10^{23}

Finally, the real chemistry!



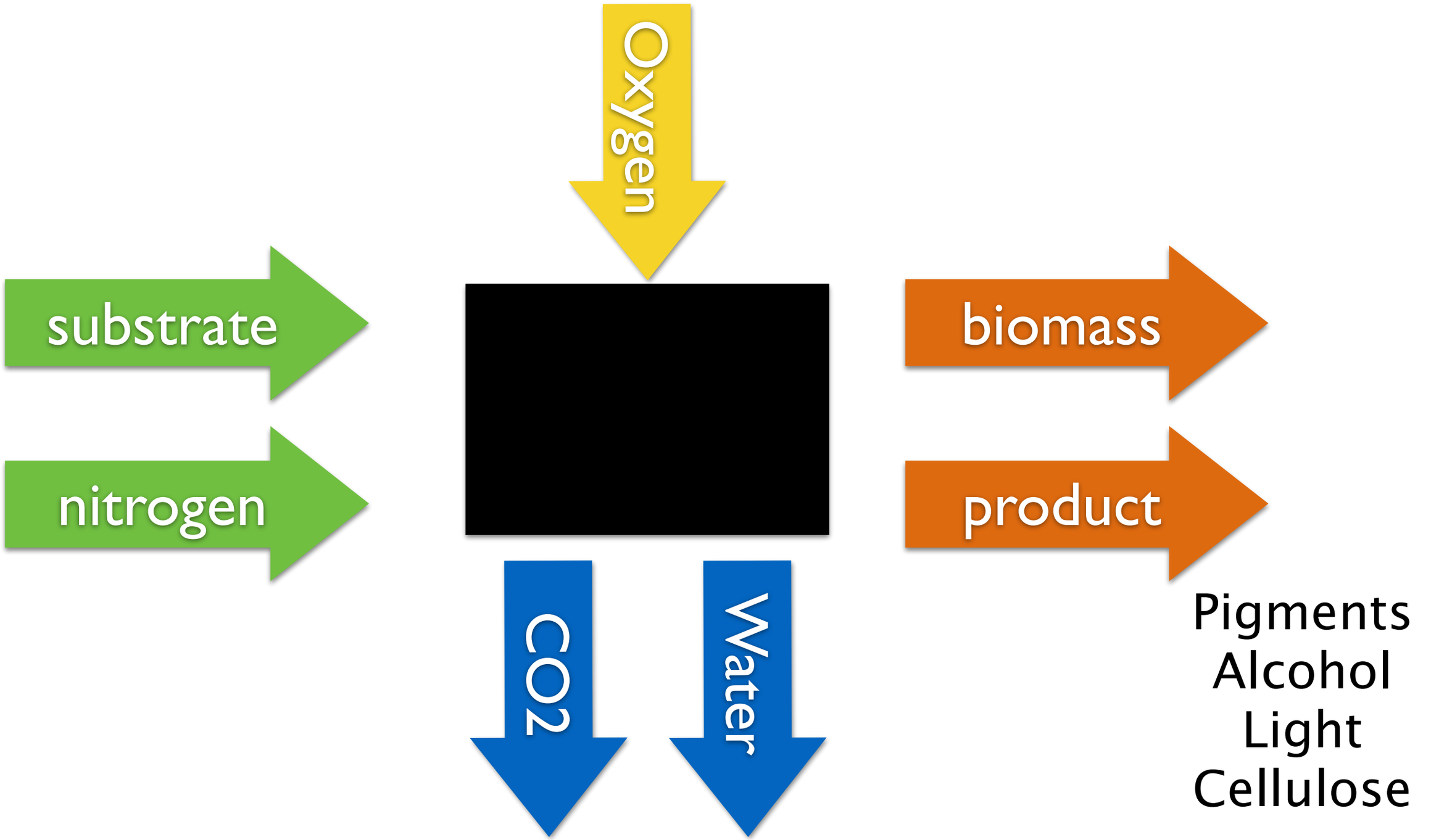
Molecular Weight of Water

Atom	Number in molecule	Atomic Weight	Total Mass
H	2	1	2
O	1	16	16

Molecular weight: 18

One mole of water: 18 grams

Black box approach



Elementary composition Lactobacillus

4,201 PROT + 0,074 DNA +
0,329 RNA + 0,015 LTA +
0,032 LIP + 0,119 PG + 0,064
POLYS + 18.15 ATP

->

BIOMASS + 18.15 ADP + 18.15 phosphate

BIOMASS: $CH_{1,95}O_{0,63}N_{0,22}P_{0,02}S_{0,01}$

BIOMASS mol weight: 27.8 g/C-mol

Oliveira, AP, et al

P. Roqueforti eating lactate

$$C_3H_5O_3^- + 3O_2 + H^+ -> 3CO_2 + 3H_2O$$

Acid is consumed