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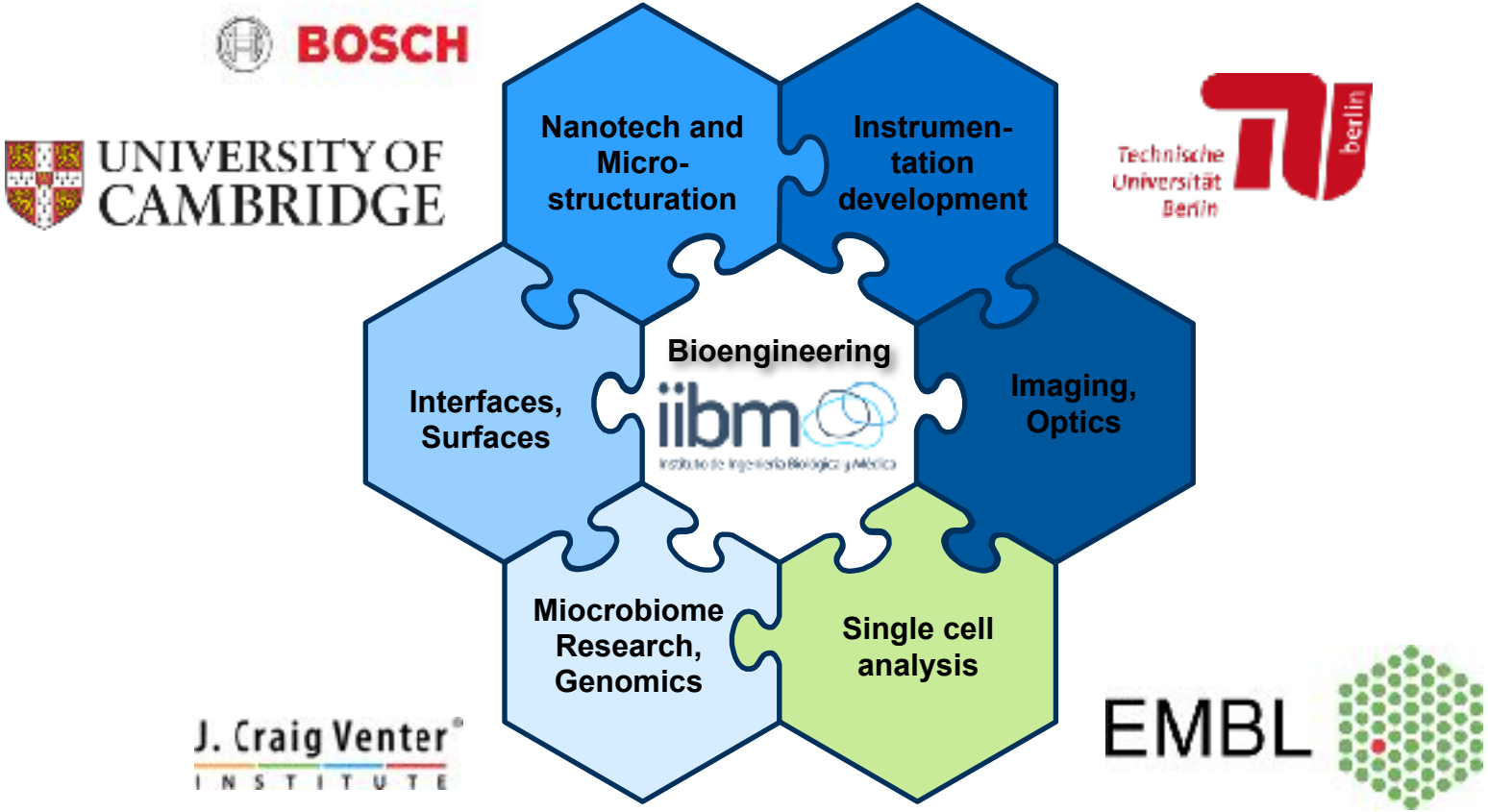
Microfluidic method development for Single-cell microbiota analysis

Asst. Prof. Dr. Tobias Wenzel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Single cell analysis
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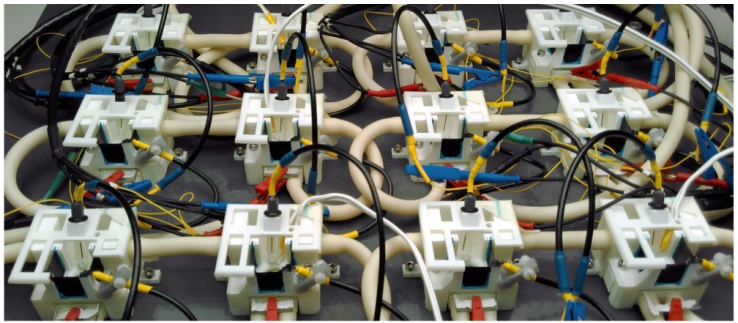
The (human) microbiome as research target

- > 50% of cells in a human are bacteria (10^{13} cells in gut)
- 99% of genes in a human are bacterial genes
- 100+ disease associations with gut microbiome composition
- Opportunity to tackle **resistant pathogens** with **microbiome interactions**

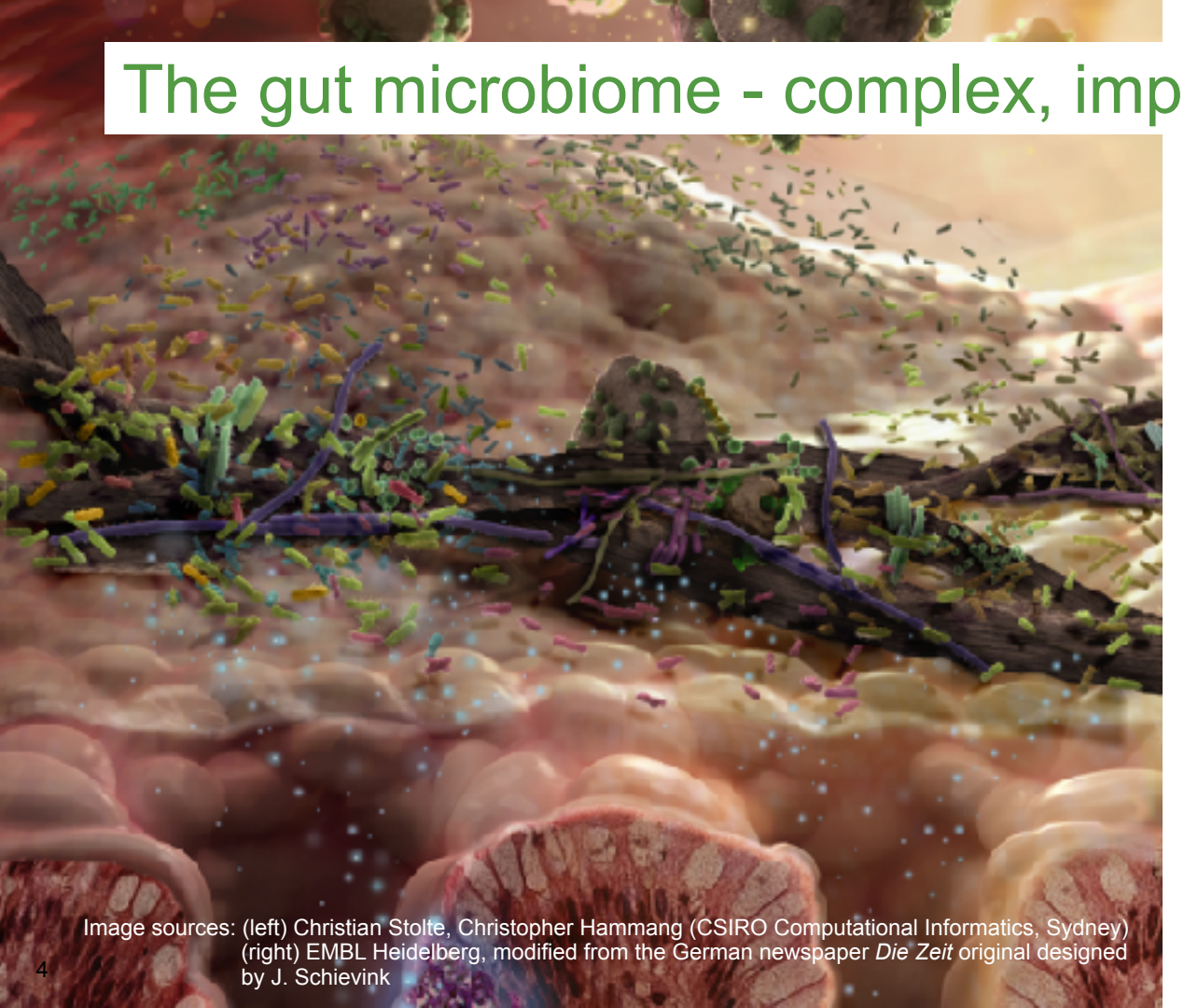
Image source: UC San Diego Health for Guardian article



Physics/Engineering perspective:

- Novel technological approaches to get data using **nano- and micro-fabrication**
- More novel data: ultra-high **throughput** experiments with **microfluidics**

The gut microbiome - complex, important



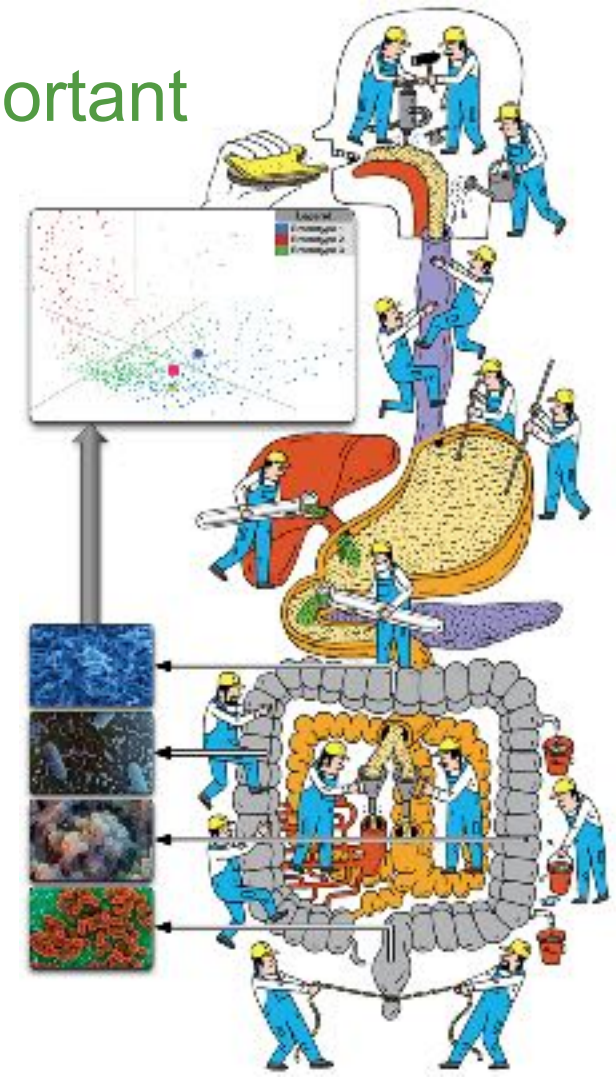
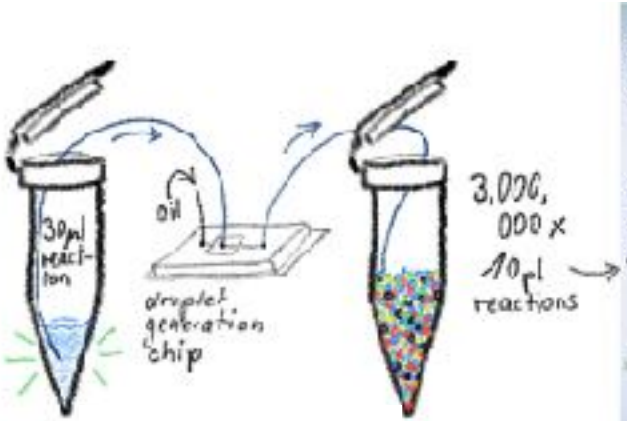
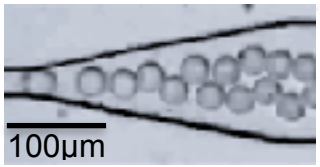


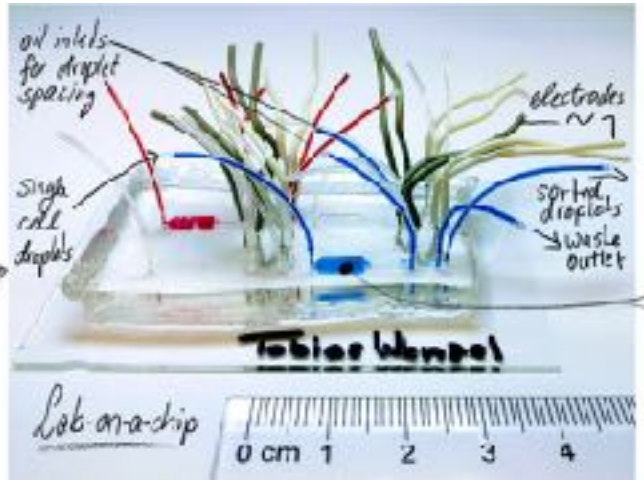
Image sources: (left) Christian Stolte, Christopher Hammang (CSIRO Computational Informatics, Sydney)
(right) EMBL Heidelberg, modified from the German newspaper *Die Zeit* original designed by J. Schievink

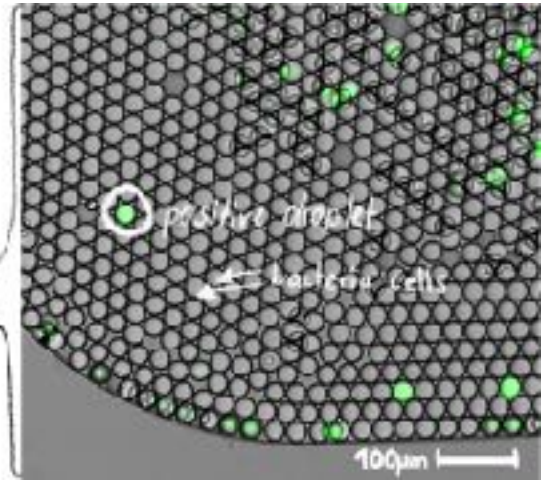
Single-cell analysis with droplet microfluidic method development

- One droplet = one experiment, e.g. with one cell each
- Experiments with millions of droplets per hour









Droplet Microfluidics

- Single cell control
- Interactions
- Ultra-high throughput
- Less contamination
- Versatile
- Reagent efficient

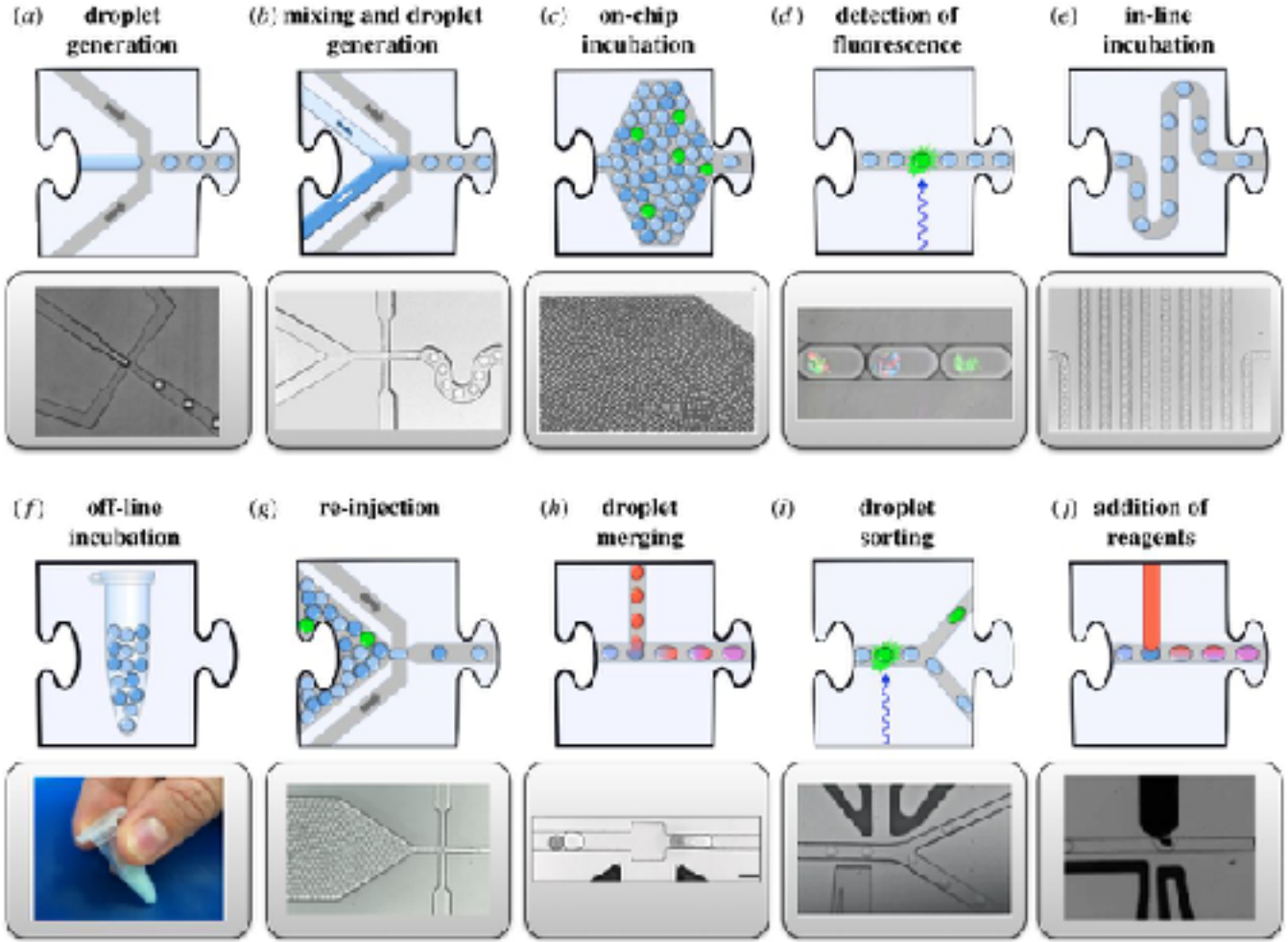
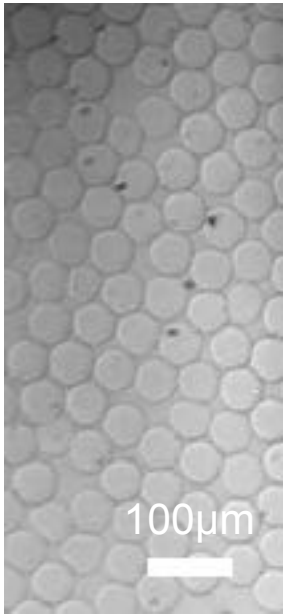
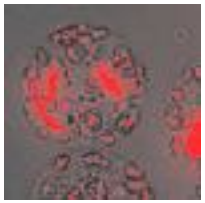


Image source: Liisa D. van Vliet et al. Interface Focus 2015

Interactions - high-throughput micro-gel (co-)culture

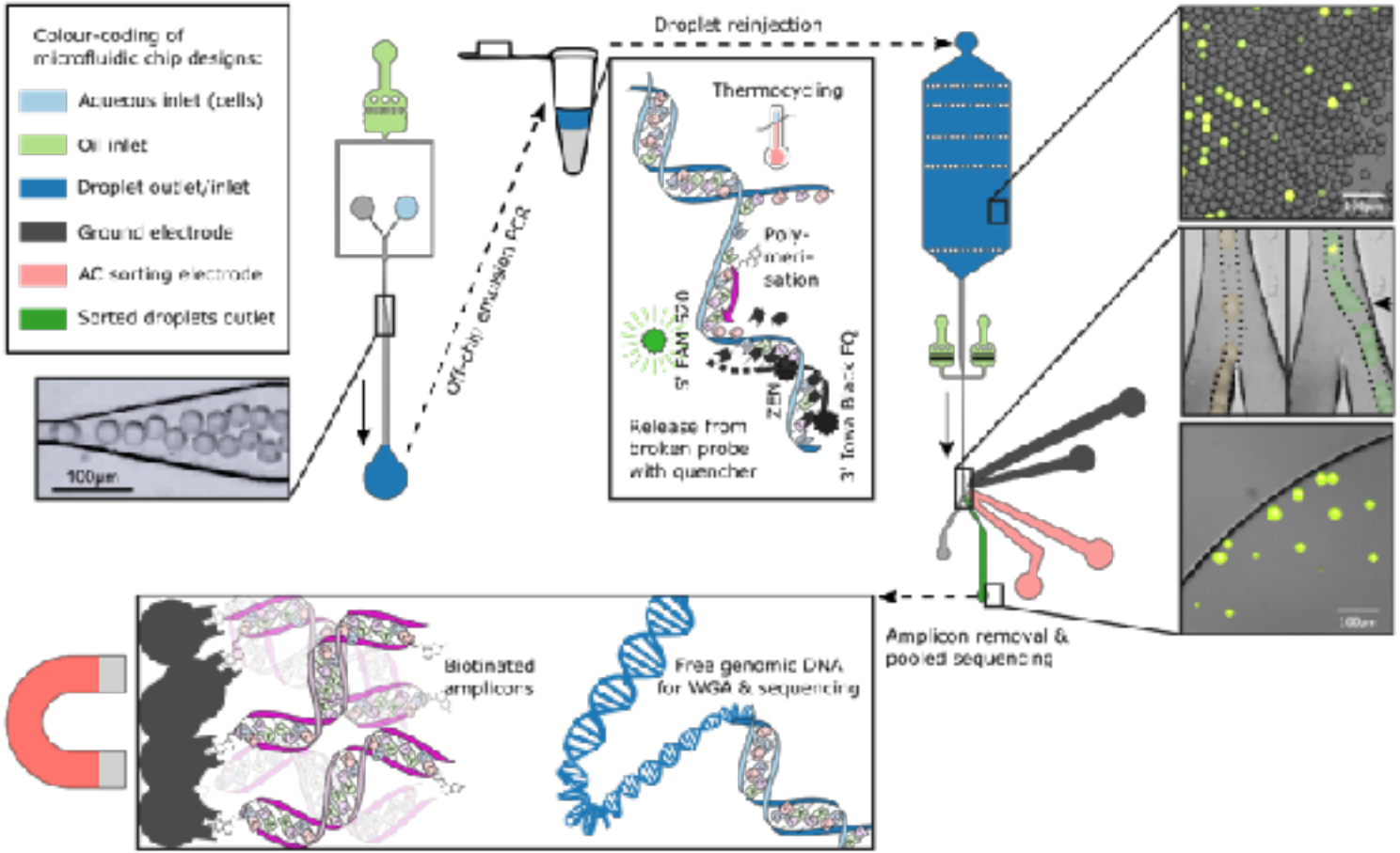


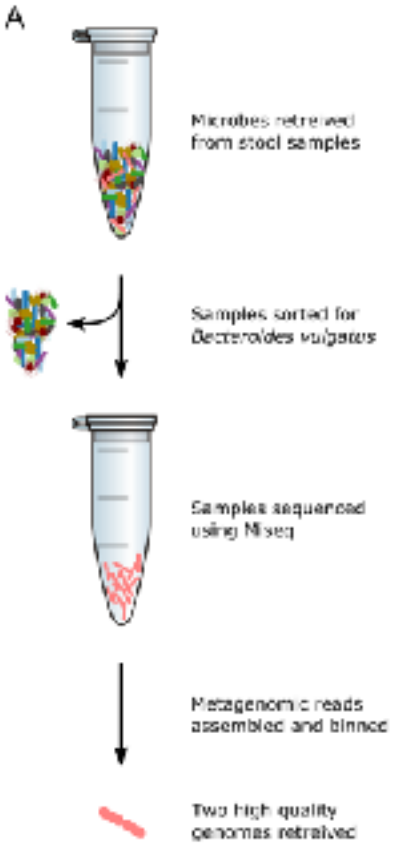


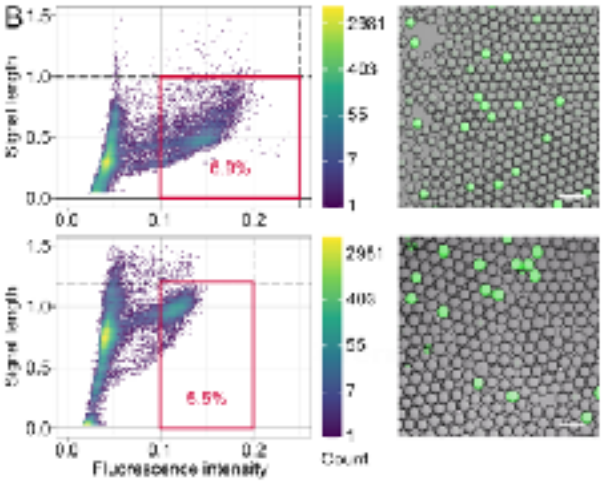
- Community functionality (resilience) - is more than individual strain properties
  - protection mechanisms, accumulation, intermediate metabolites, emergence
- Interactions are essential for cultivability
- Novelty: no systematic knowledge and use

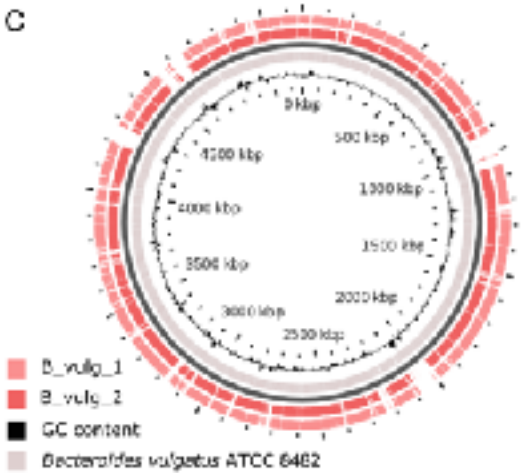
Tackling antibiotic resistance with microbiota interactions

Precision Genomics: Enriching gut microbiome strains for cultivation-free genome sequencing using droplet microfluidics









Cell Reports Methods

ARTICLE | ONLINE NEW 100137

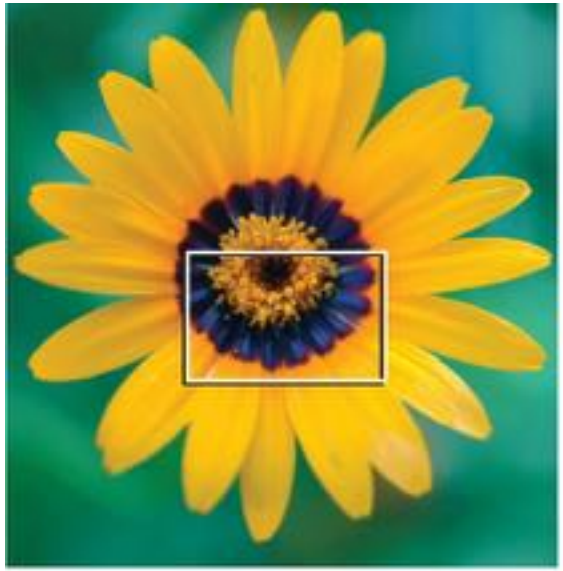
Enrichment of gut microbiome strains for cultivation-free genome sequencing using droplet microfluidics

Anna Pyzocak [1] • Tobias Werner [1] • Kiley West Seitz • Falk Hildebrand • Eva Kaisal • Marco Raffaele Cosenza • Vladimir Benes • Peer Bork [2] ✉ • Christoph A. Merten [2] ✉ • Show less • Show footnotes

Open Access • Published: December 29, 2021 • DOI: https://doi.org/10.1016/j.crmeth.2021.100137

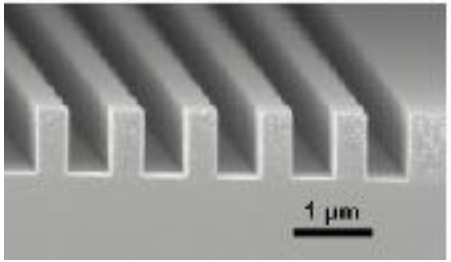
Microfabrication and Bio-Nanotechnology

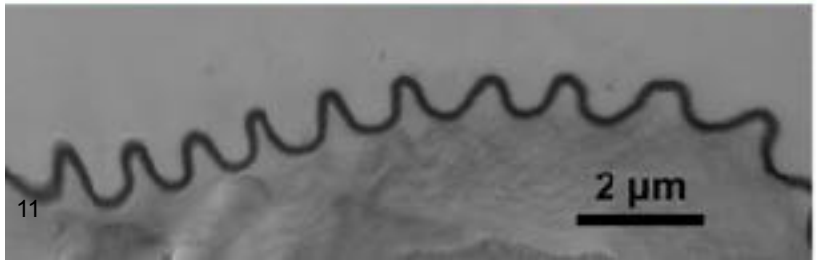
Understanding of natural "engineering principles" biomimicry

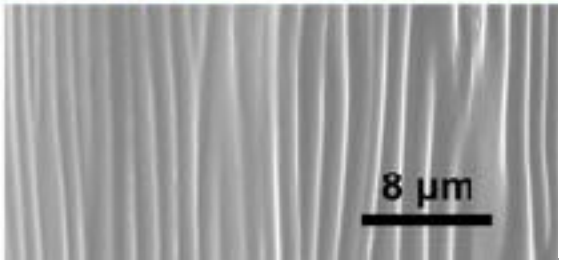


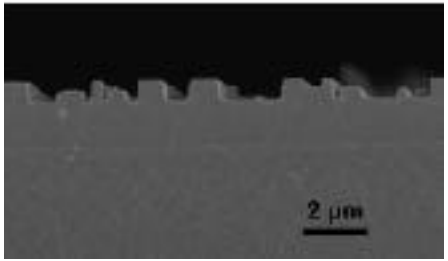
nature

E. Moyroud* & **T. Wenzel***, et al.; *Nature* 550, 469-474 October 2017

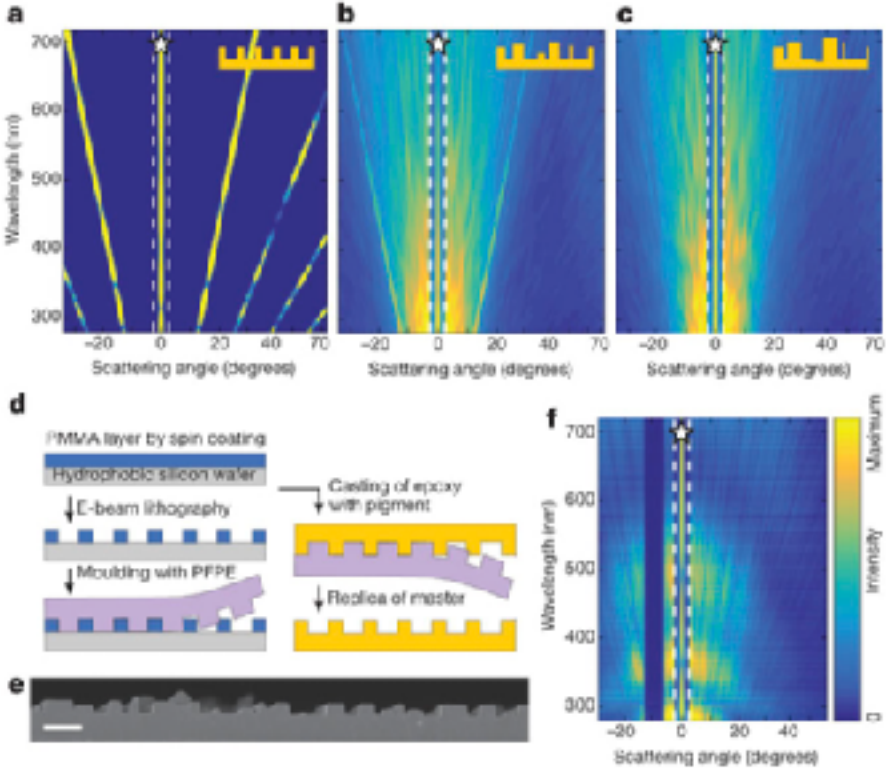


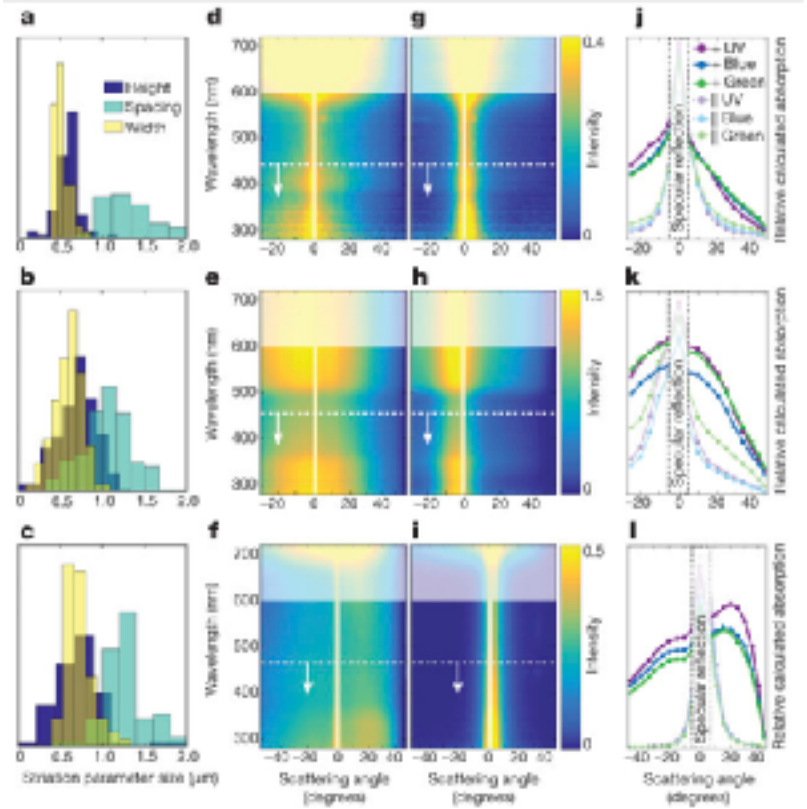






Coding for super-computer simulations





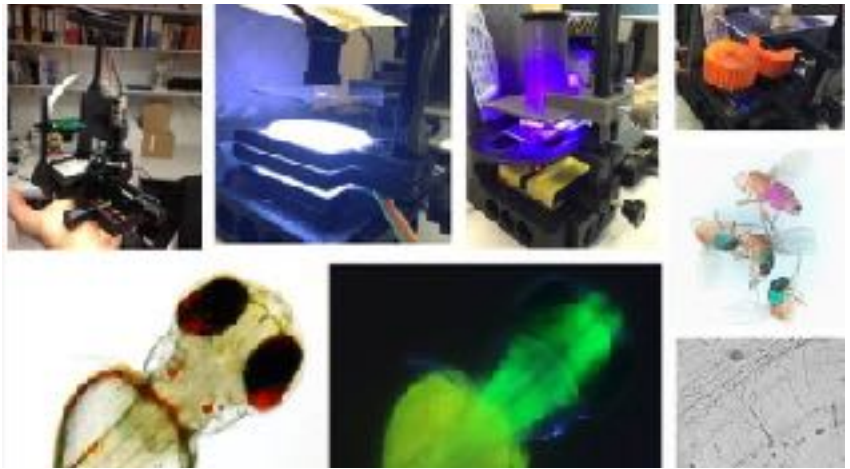
Upcoming: open source microfluidic workstation

3D printed fluorescence microscope

PID temperature controller/stirrer/sample holder

RPi-hat for flow and strobe controls

Low-cost high-end instrumentation
access + automation = reproducibility



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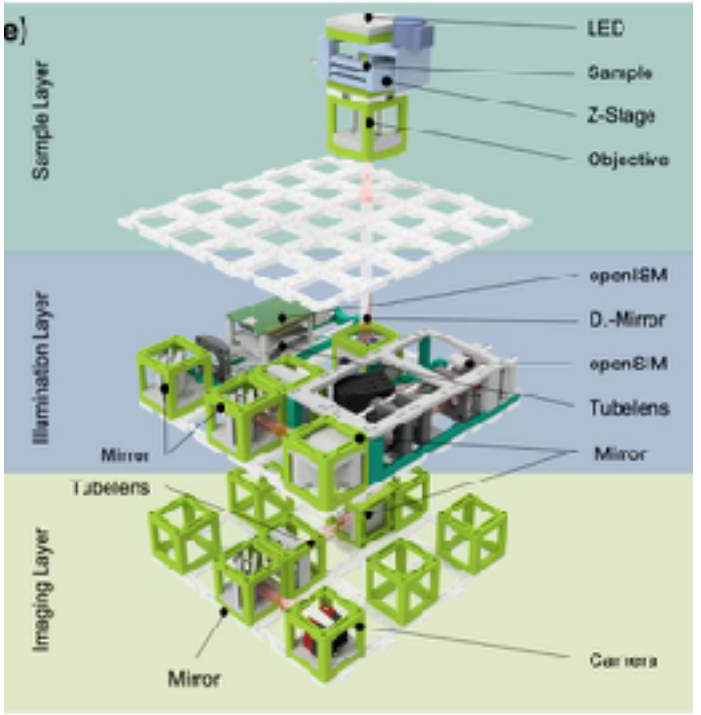

<- FlyPi

“If I have seen further it is by standing on the shoulders of Giants"

Sir Issac Newton

- Build creative tools that address new custom problems
- Reduction of cost
- Maintaining the equipment in-house
- Easy to automate and work with useful data formats
- Better collaborations - reproducibility, agile exchange

¡Gracias! Let's discuss…

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Image source: Evan Ingersoll & Gael McGill (Digizyme Inc, Brookline MA)