

Magnetotactic Bacteria Bioprocessing

Magnetotactic bacteria bioprocessing and digitalisation webinar

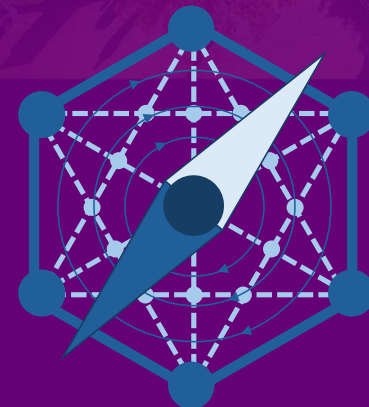
24th June 2026

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MagBI



Magnetotactic bacteria and Magnetosomes

Magnetotactic bacteria (MTB)

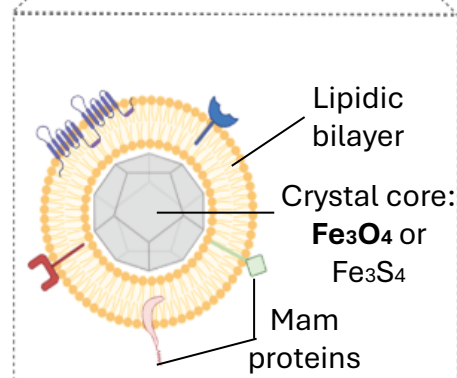
*Magnetopirillum
gryphiswaldense* MSR-1

PHA granules – MTB store energy in form of polyhydroxyalkanoate (PHA) granules.

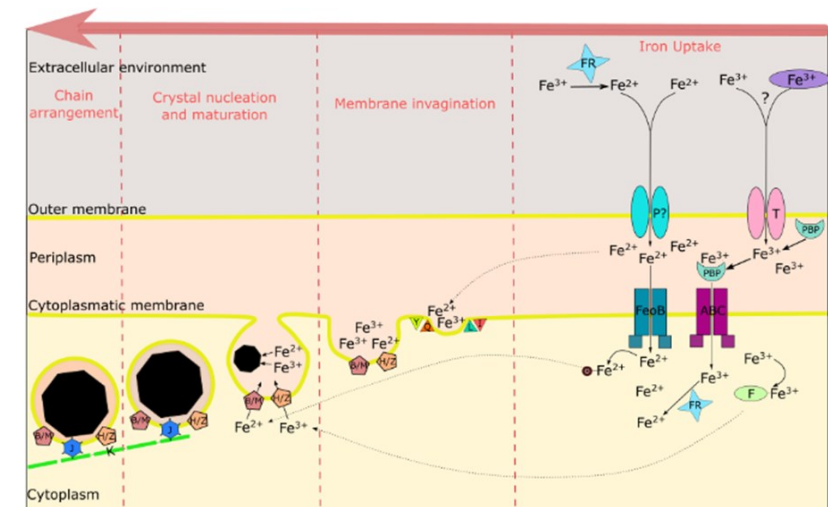
Magnetosomes – serve as navigational compass needles allowing MTB to migrate along redox gradients through the earth's geomagnetic field lines

Magnetosome chain

Magnetosome structure



Magnetosomes are synthesized through a complex **biomineralization** process.



(Masó-Martínez et al., 2022)

Magnetosome properties

Synthetic routes for Magnetic Nanoparticles (MNPs)

Chemical
(90%)

Physical
(8%)

Biological
(2%)

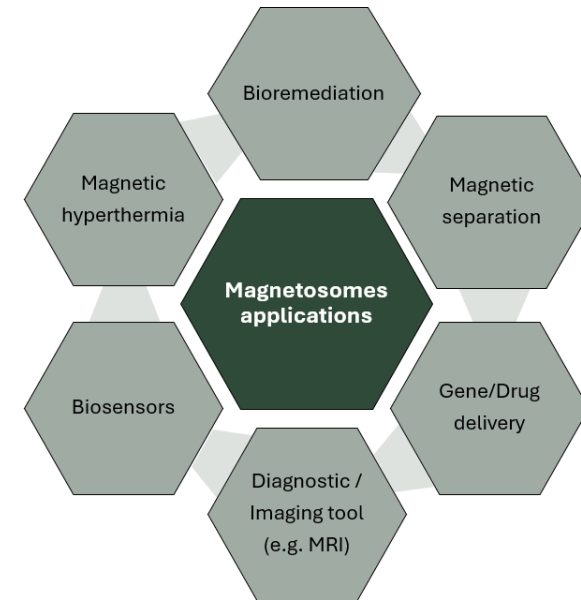
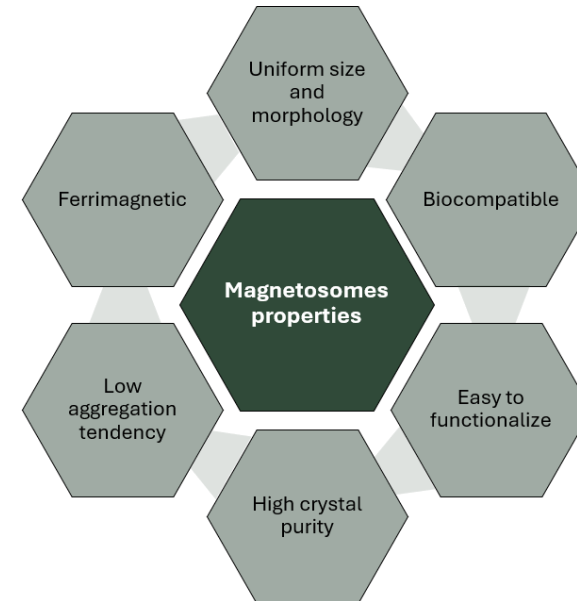
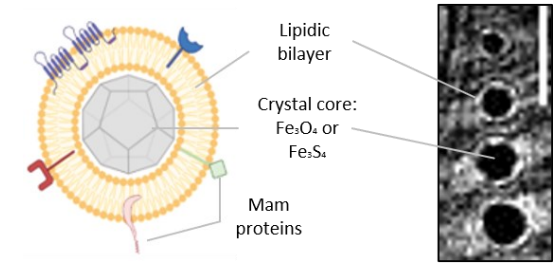
Common issues ☹️

- ✖ Complexity → High expense
- ✖ Extreme temperature &/or Pressure
- ✖ Oxygen – tight control or elimination
- ✖ Chemical waste (solvents, surfactants)
- ✖ Poor yields
- ✖ Difficult scale-up
- ✖ 'Batch-to-batch' variation (size, microstructure, composition, impurities)
- ✖ Product instability (dissolution, oxidation, colloidal instability/aggregation)
- ✖ **Need for coating / modification / functionalization steps post-manufacture**

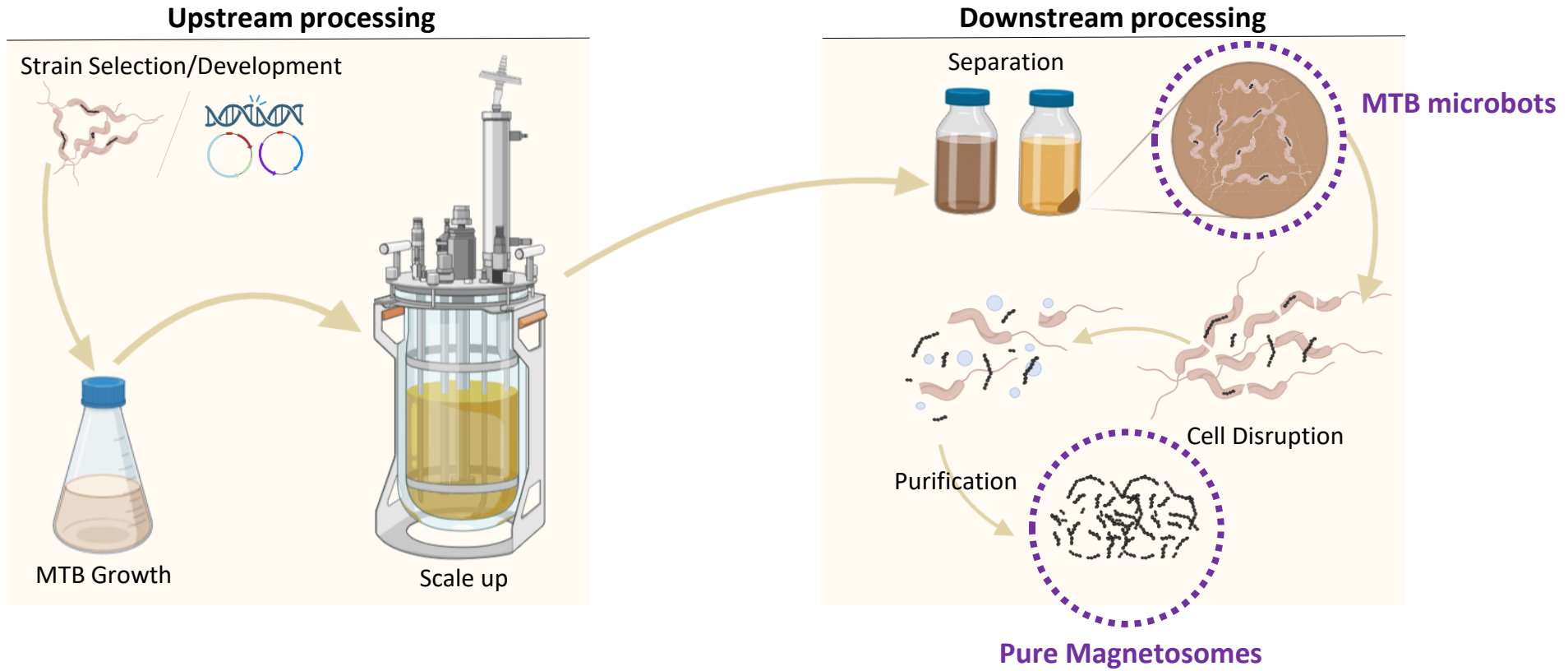
MOs & plants – Metal ion uptake & biological reduction

In vitro – e.g., using extracts from sulphur reducing bacteria, or artificial biomineralization proteins of bacterial origin

Greener solutions to making MNPs



MTB Bioprocessing

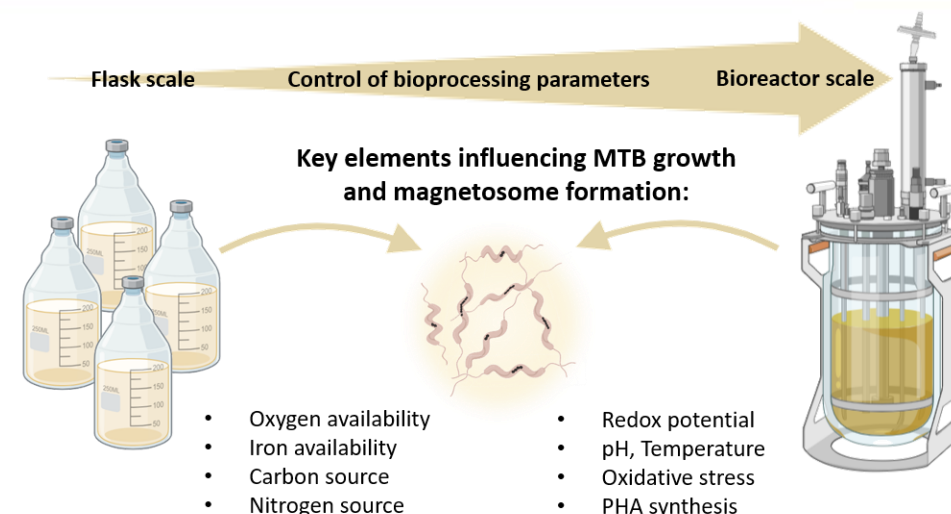




Challenges of MTB bioprocessing

The challenge:

- Magnetosome **productivity is low** compared to chemical synthesis of magnetic nanoparticles.
- There is **relatively low understanding** about the MTB metabolism and physiology.
- Need to ensure **product quality**.



Summary of magnetosome and cell **yields** of various MTB strains cultured using different **strategies** and culture media.

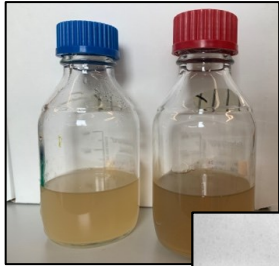
Strain	Cultivation strategy	Medium	Scale (L)	Cell yield (g DCW L ⁻¹)	OD ₅₆₅	Magnetosome yield (mg Fe L ⁻¹)	Reference
MSR-1	Batch	FSM	4	0.4	1.4	7.9	Heyen et. al 2003
AMB-1	Batch	FSM	4	0.48	2.5	4.7	Heyen et. al 2003
MSR-1	Fed-Batch	OFM	42	2.17	7.24	41.7	Sun et al. 2008
MSR-1	pH-stat	OFM	42	-	12.2	83.23	Liu et al. 2010
MV-1	Batch	OGM	5	-	-	64.35	Silve et al. 2013
MSR-1	Semicontinuous	OFM	42	9,6	42	356.52	Zhang et al. 2011
MSR-1	Semicontinuous	OFM	7.5	7.59	30.4	225.53	Zhang et al. 2011
MSR-1	Fed-batch	MGM	40	2.4	8	10	Berny et al. 2020
MSR-1	pH-stat	FSM	5	4.2	16.6	54.3	Fernández-Castané et al. 2018

OFM = Optimized flask medium; OGM = Optimized growth medium; MGM = Minimal growth medium; FSM = Flask Standard Medium.



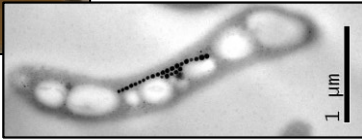
MSR-1 Bioprocessing strategy and workflow

Inoculum



Seed culture
~300 ml
Aerobic
conditions

MSR-1



5L Bioreactor



pH-stat
strategy

(Fernandez-Castane, et al., 2018)



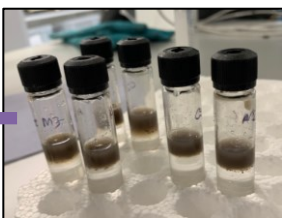
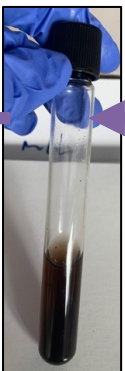
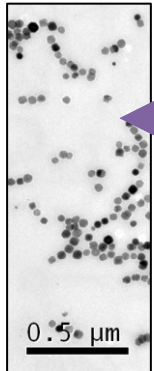
Cell harvesting



Fermentation broth is
centrifuged



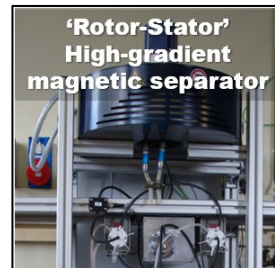
Magnetosome purification



Gradient density
ultracentrifugation

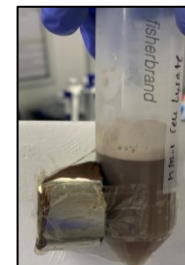


Magnetic separation



RS-HGMS
0.28 T

(Fernandez-Castane, et al., 2024)



Cell disruption



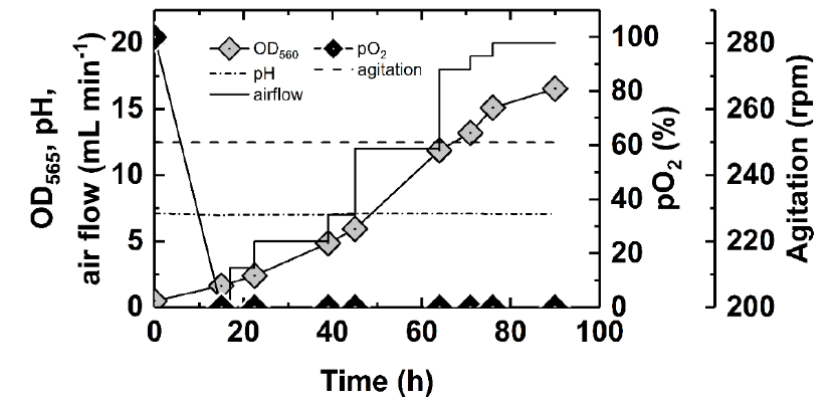
High pressure
homogenizer
1 pass at 10 kpsi

(Fernandez-Castane, et al., 2024)

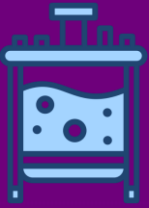


MSR-1 pH-stat strategy

- Media: Flask Standard Medium (FSM) – without iron
- Temperature: 30°C
- pH 7: controlled by acid feeding solution → Lactic acid (100 g/L) , iron, sodium nitrate (25 g/L)
- Stirring: 150-400 rpm
- $pO_2 \rightarrow 0.1\%$ set point (cascade control)
- Aeration strategy:
 - Start without air supply (“aerobic” conditions)
 - pO_2 drops to 0.1% (set point) → start aeration
 - Keep increasing air flow as O_2 demand increases.



(Fernandez-Castane, et al., 2018)



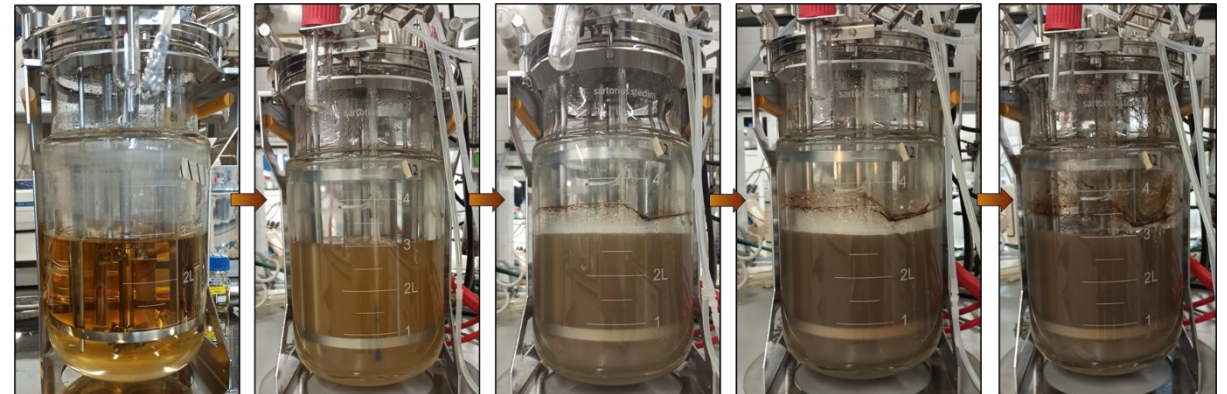
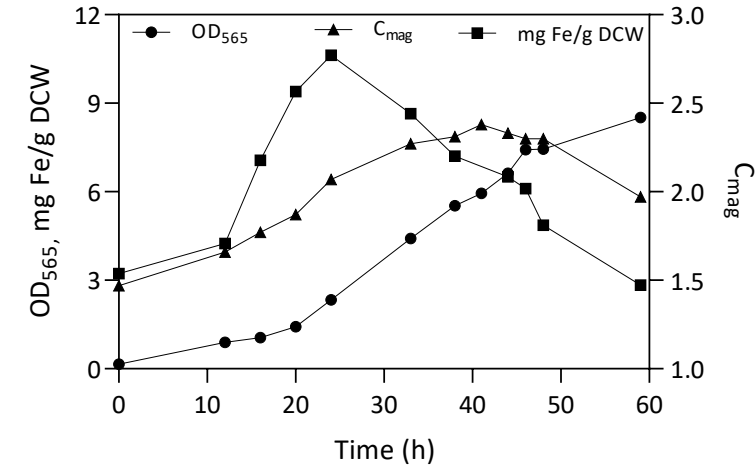
Monitoring strategy

Parameters controlled by DCU:

- Temperature
- pH
- Volume of feeding added
- O₂ concentration (pO₂)
- Stirring
- Air flow (mL/min)

Parameters monitored:

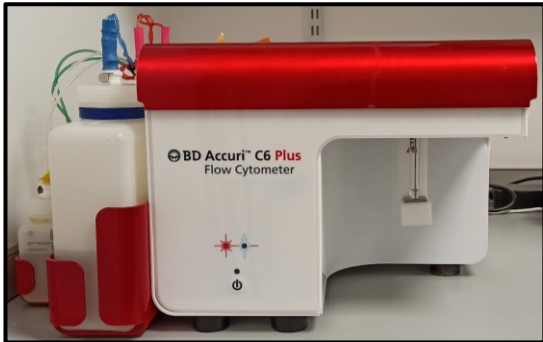
- Bacterial growth (OD₅₆₅) → in-line
- Cellular magnetic response (C_{mag}) → in-line
- Lactate concentration → in-line
- Extracellular and intracellular iron concentration → off-line (ICP-OES)
- CO₂ and O₂ gases → in-line
- Cell morphology (microscopy) → in-line
- Bacterial physiology → in-line (FCM)



FCM as a tool to track cellular physiological changes

Monitoring the physiological properties during cell growth can help to understand the dynamics of cell growth and magnetosome formation.

Flow Cytometry



(Fernandez-Castane, et al., 2018)

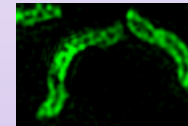
Physiological parameters

Membrane polarization and cellular death

- **PI** (propidium iodide) → **Dead/Alive** cells
- **BOX** (DiBAC₄(3) Bis-(1,3-dibutylbarbituric acid) trimethine oxonol) → **Membrane polarisation**

Soluble **intracellular iron pool** (Fe²⁺)

Phen Green™ SK



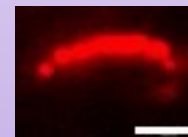
Accumulation of **PHA aggregates**

- **Pyr-546** (pyrromethene-546)

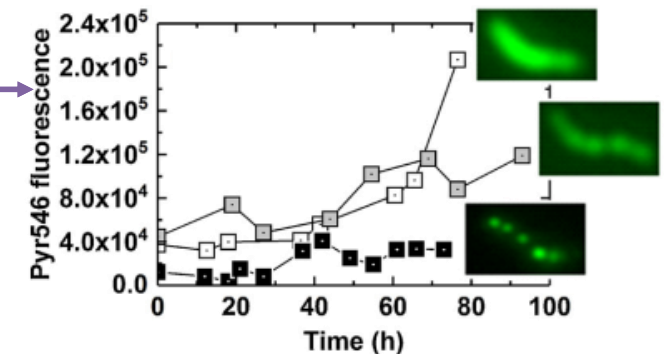
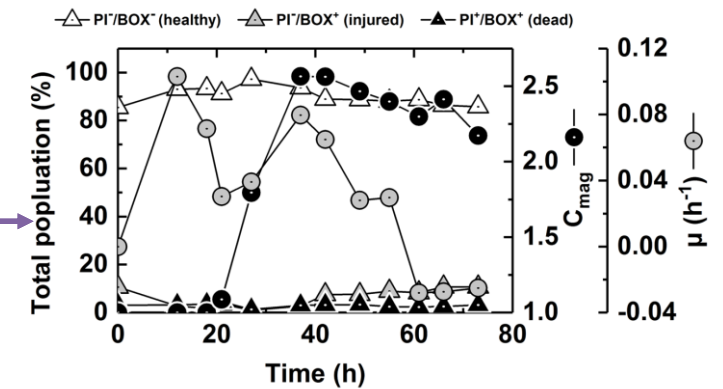


Accumulation of **intracellular ROS**

- **CellROX™ Deep Red (CRDR)**



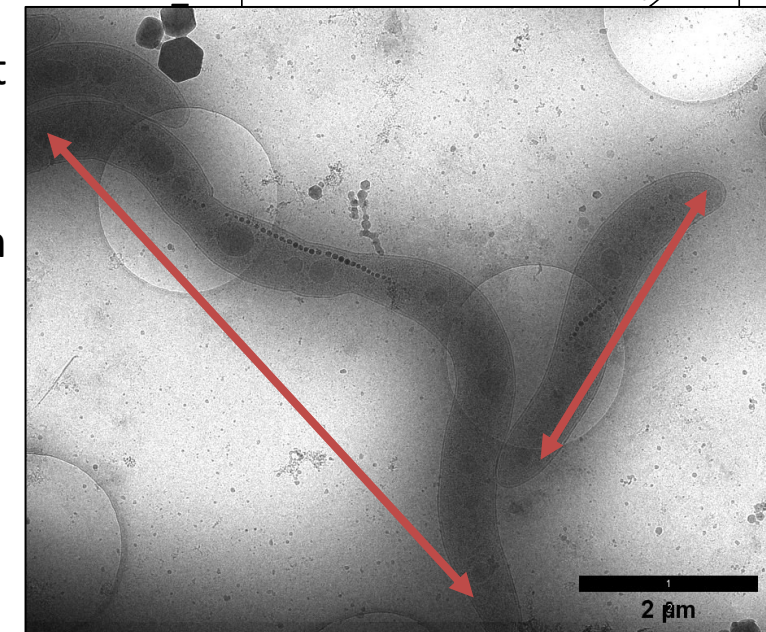
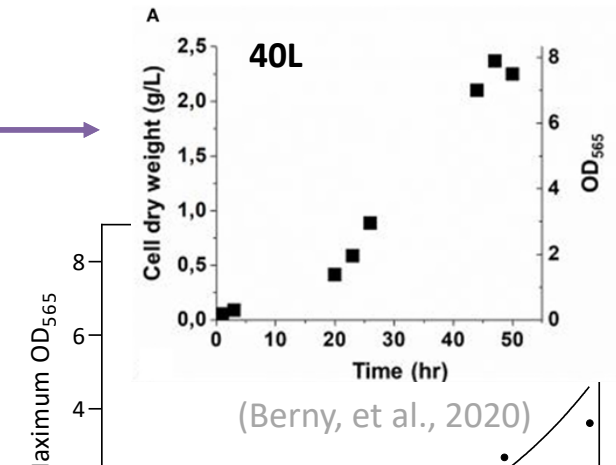
(Masó-Martínez et al., 2025)





Challenges for MTB microbots bioprocessing

- For medical applications → Removal of toxins from the media is a requirement.
- Bacteria harvesting → gentle systems to preserve membrane stability.
- Real-time monitoring bacteria physiology (e.g. bacterial fitness during seed culturing).
- Find suitable solutions to preserve the stability and viability of the microbots that are suitable for medical applications.
- Heterogeneity of cell sizes among microbot production → batch-to-batch variability
- Pharmaceutical/Medical Regulations



Thank you for your attention!

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