Microfluídica

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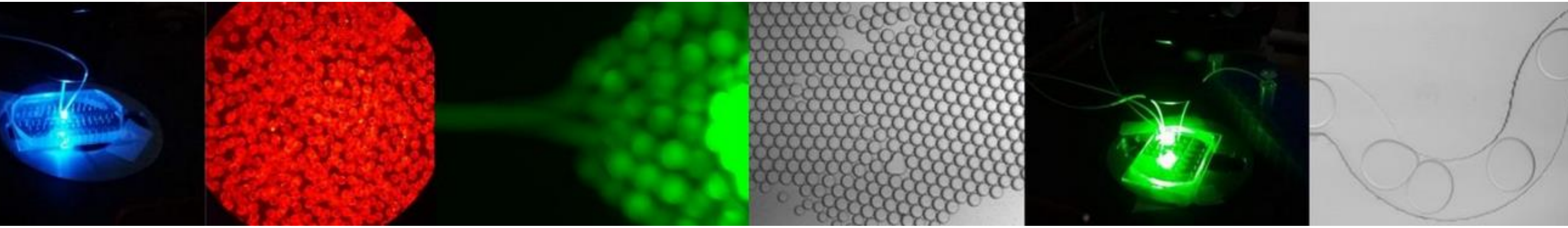
UNICAMP

40 anos Engenharia Química UNICAMP

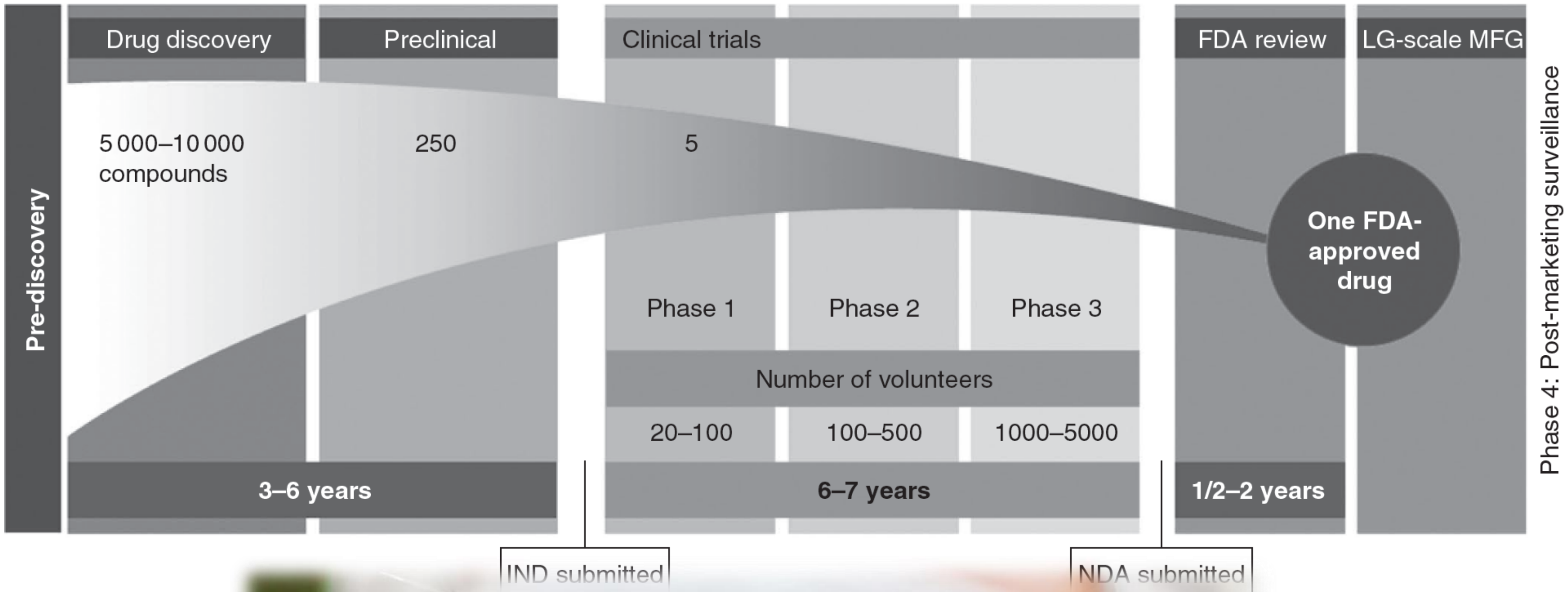
LaNBDA

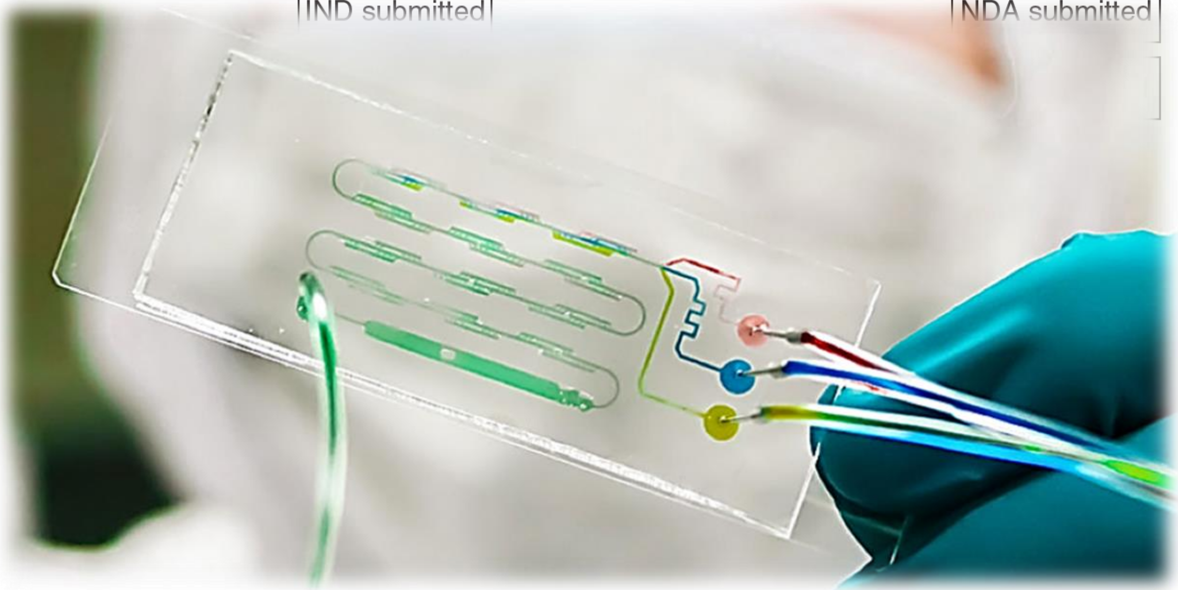
Laboratório de Nano & Biotecnologia para Desenvolvimentos Avançados

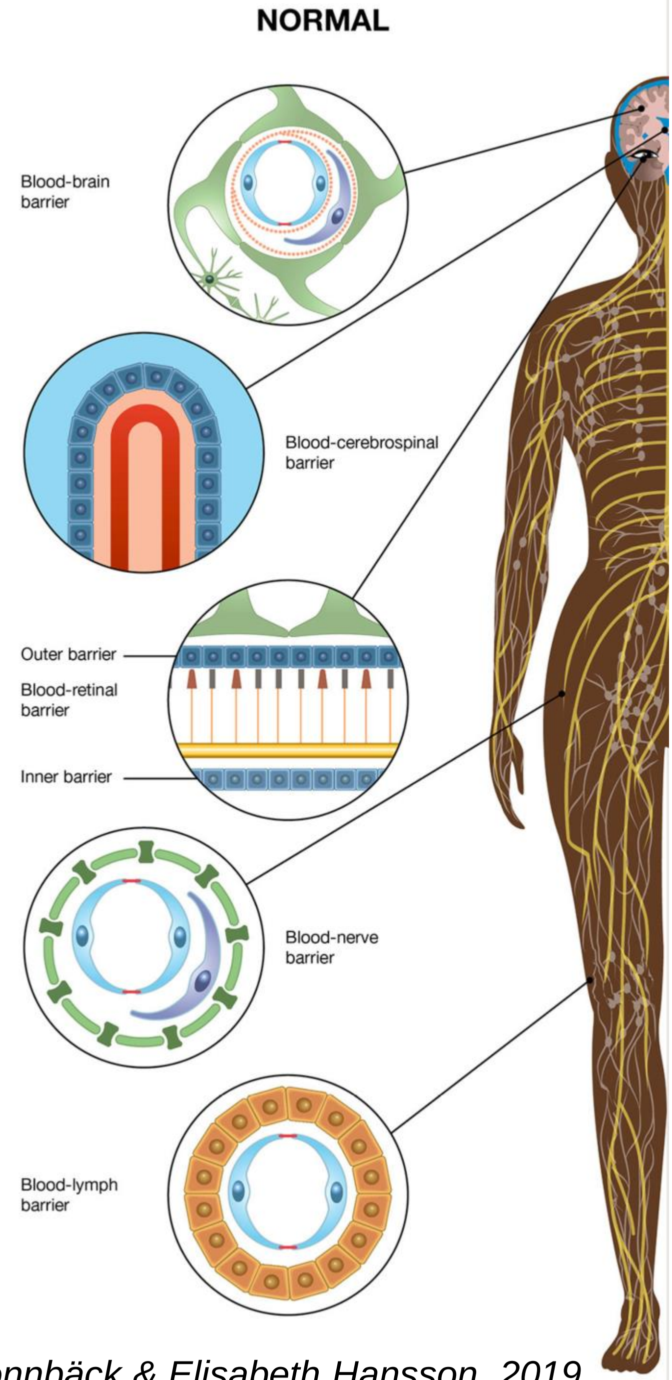


Alguns fatos...

Fonte: DAVID J. AM ENDE & MARY T. AM ENDE. ***CHEMICAL ENGINEERING IN THE PHARMACEUTICAL INDUSTRY: AN INTRODUCTION, 2019***



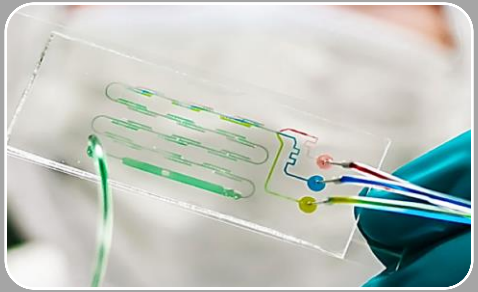




Cecilia Rönnbäck & Elisabeth Hansson, 2019

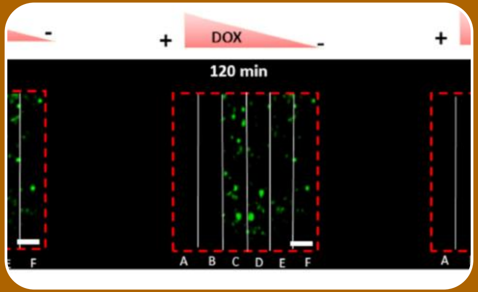
Sumário

https://vaccoat.com/blog/applications-of-plasma-treatment-in-microfluidics/



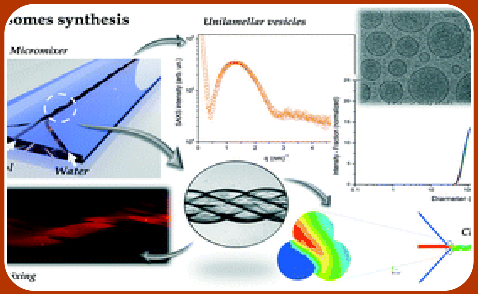
Microfluídica

- Definição
- Principais estratégias de microfabricação
- Diferentes aplicações



Microfluídica & Células

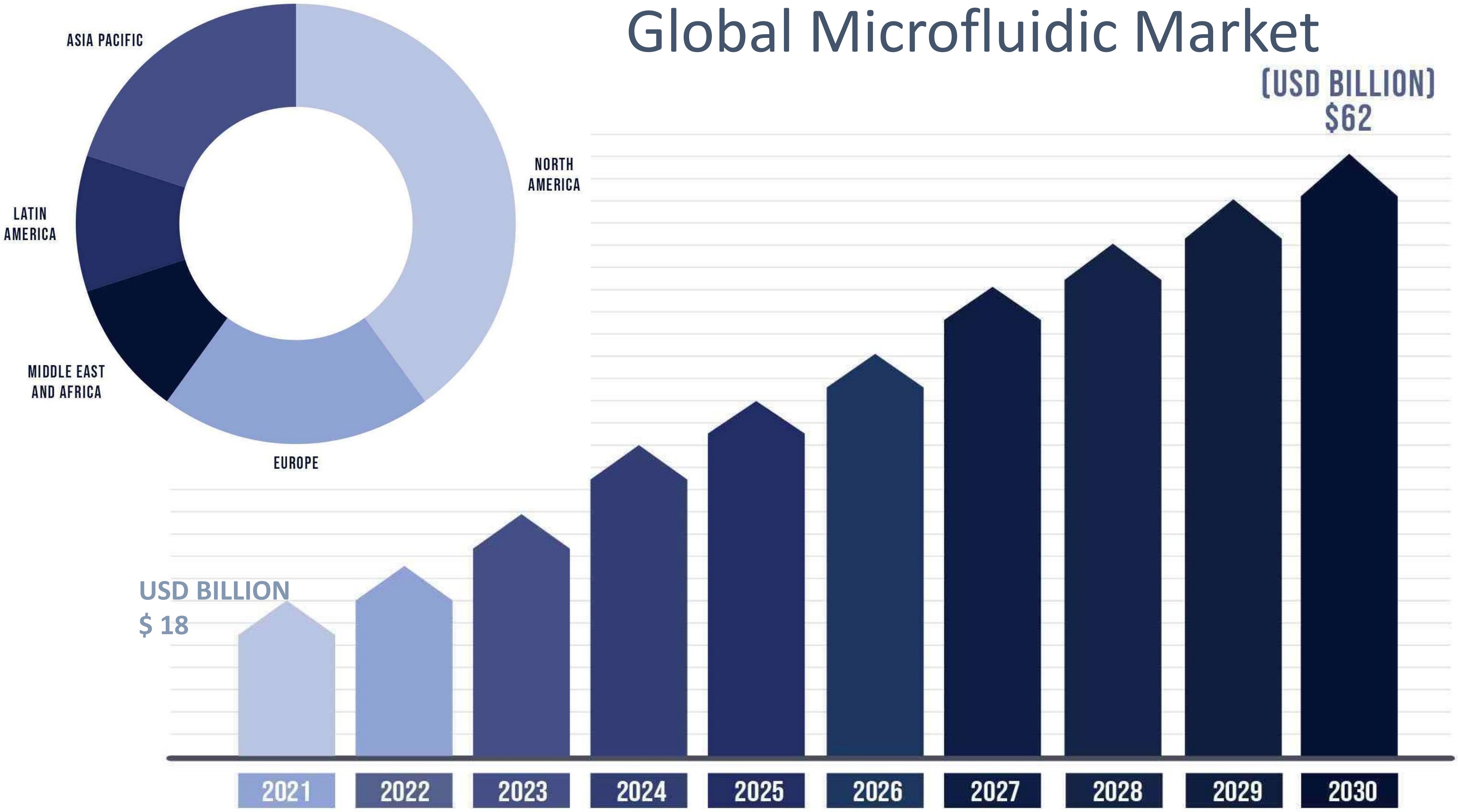
- Screening de fármacos
- Microgéis
- Tumor on a chip
- Organ on a chip



Microfluídica & Nanotecnologia

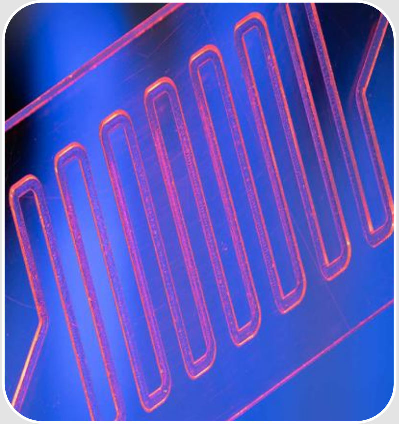
- Síntese de lipossomas
- Advecção caótica – aumento de produtividade

Global Microfluidic Market



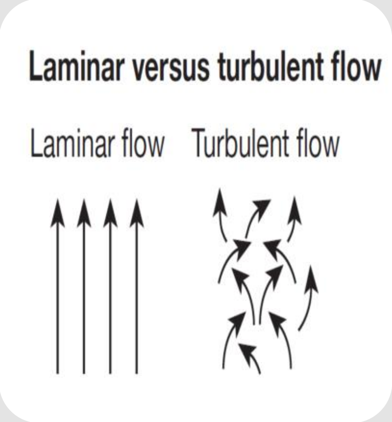
https://www.precedenceresearch.com/microfluidics-market, 2022

Microfluídica - conceitos



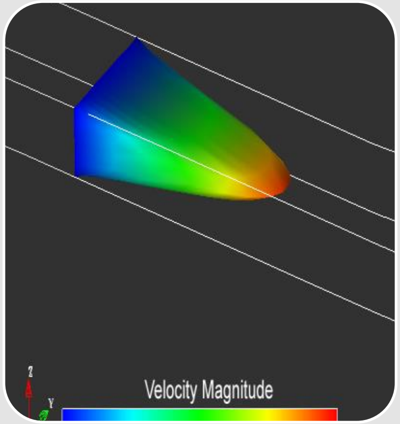
Escoamento em microcanais

https://www.drugtargetreview.com/article/91542/how-microfluidics-can-automate-drug-discovery-and-development/, 2022



Predominância de escoamento laminar

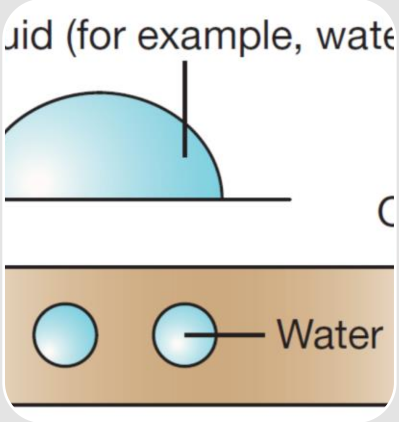
Sackman, 2014



Escoamento com perfil de velocidade

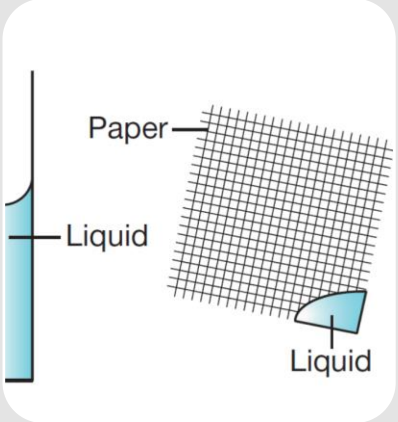
Difusão

https://faculty.washington.edu/yagerp/microfluidicstutorial/basicconcepts/basicconcepts.htm, 2022



Tensão superficial

Sackman, 2014



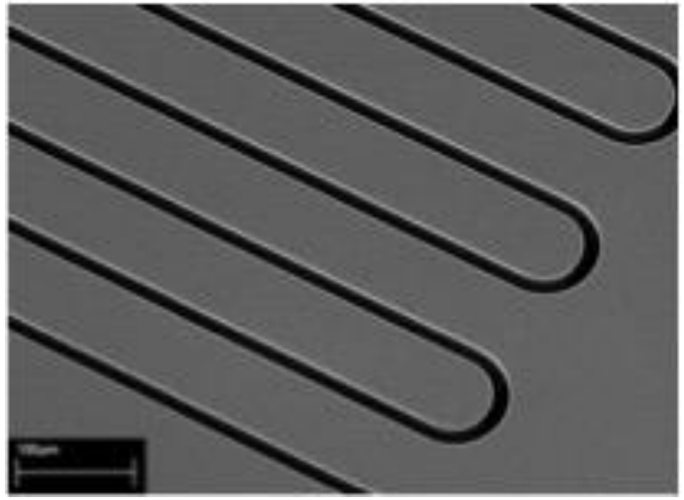
Forças capilares

Sackman, 2014

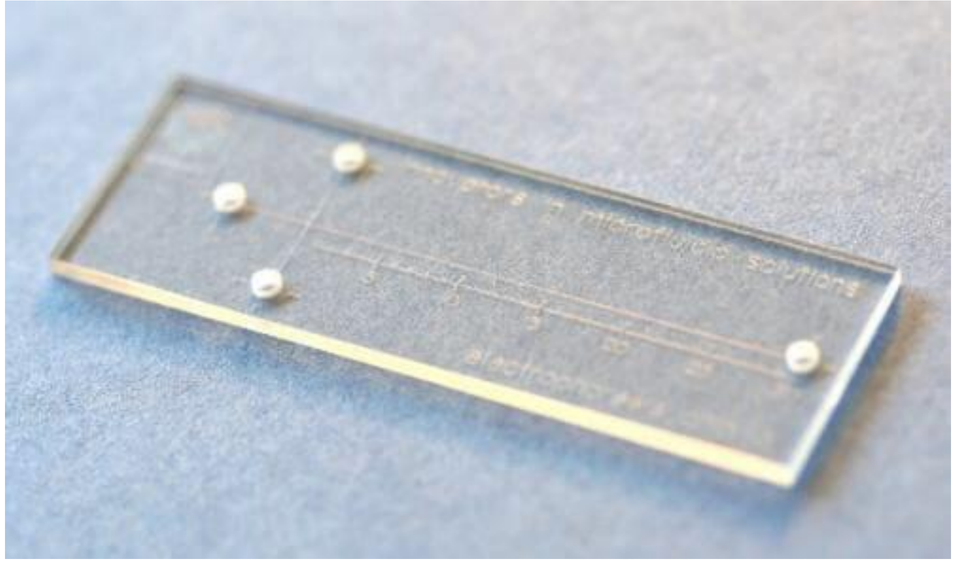
Materiais INORGÂNICOS para construção

Silício

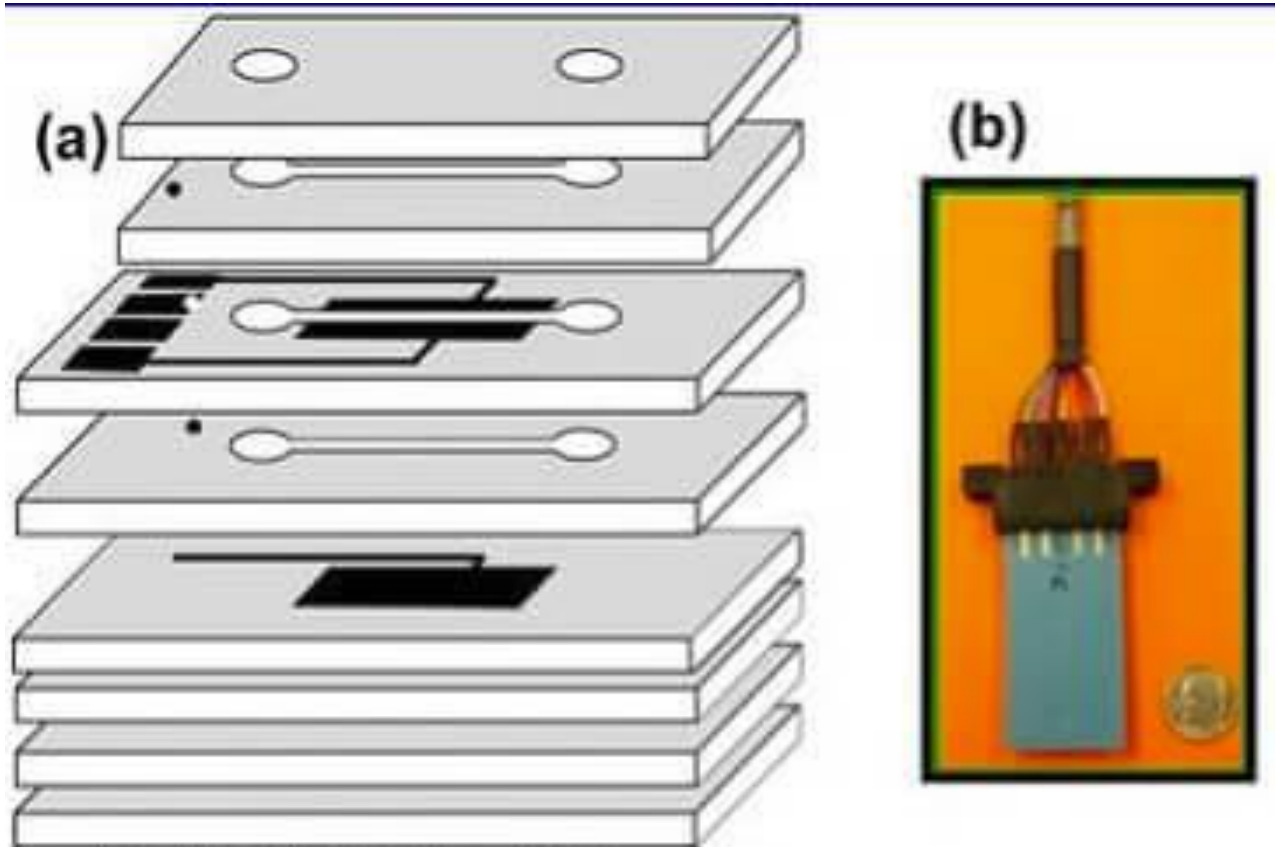
https://www.micralyne.com/technology-platforms/microfluidics-silicon-microfluidic-mems-process/



Vidro



Cerâmica

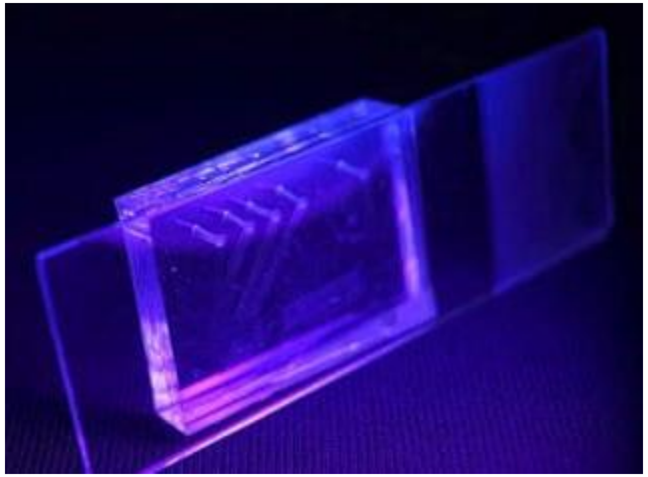


https://www.elveflow.com/microfluidic-reviews/general-microfluidics/materials-for-microfluidic-chips-fabrication-a-review-2017/

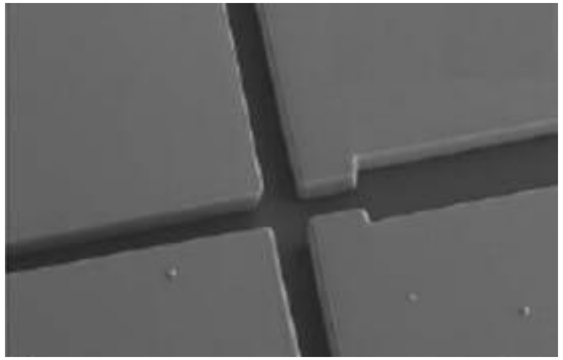
Materiais ORGÂNICOS para construção

Elastômeros

PDMS - Polidimetilsiloxano

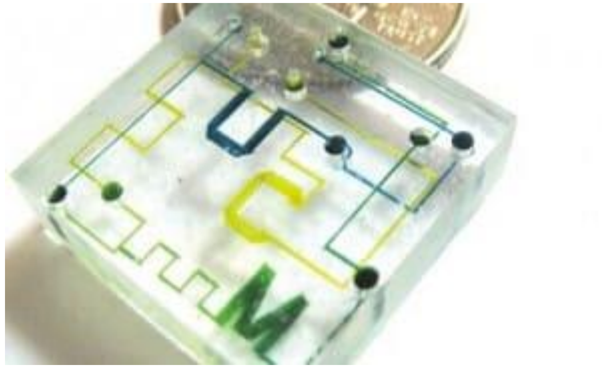


TPE - Poliéster termofixo

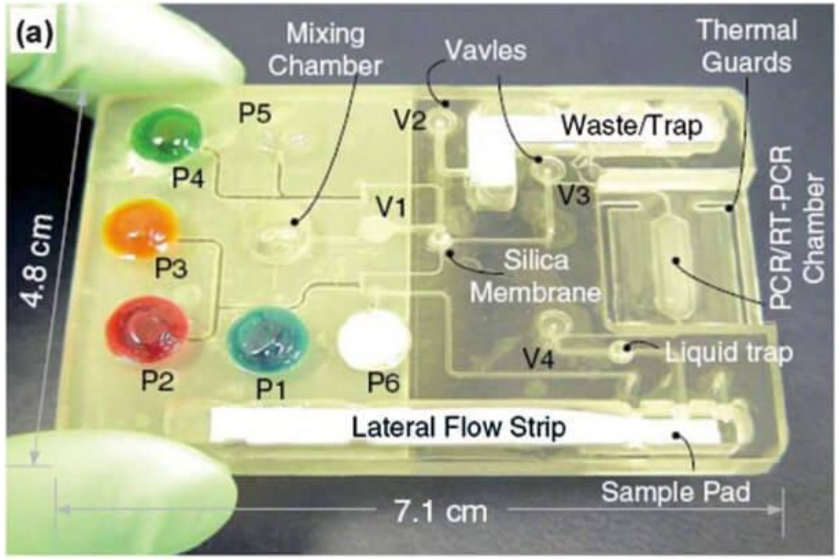


Termoplásticos

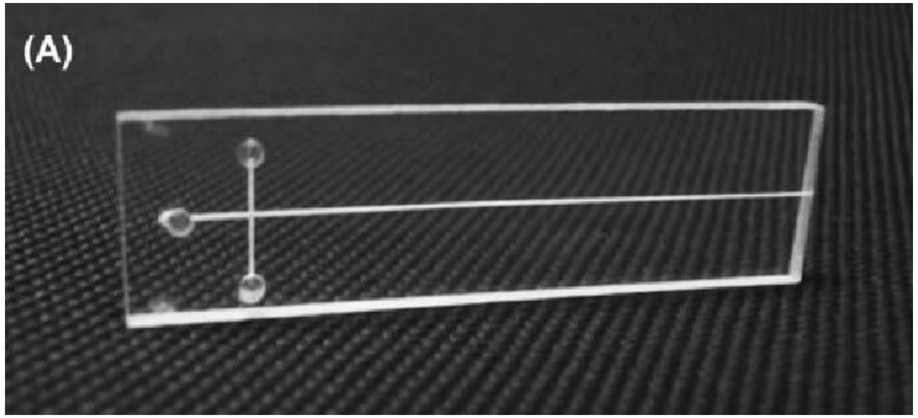
PS - Poliestireno



Policarbonato



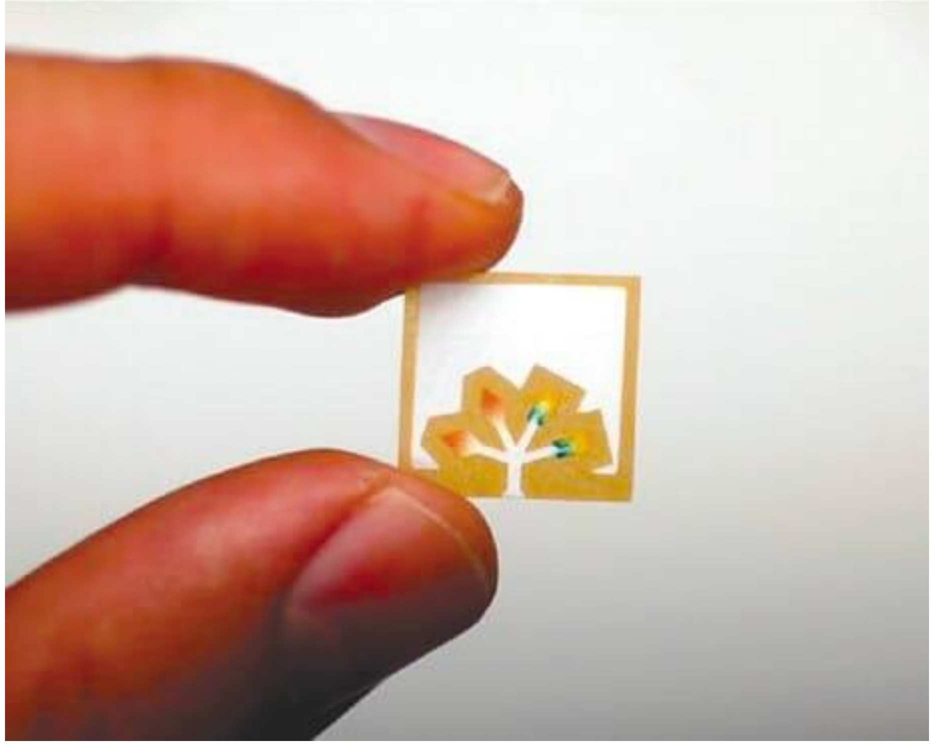
PMMA
Polimetilmetacrilatio



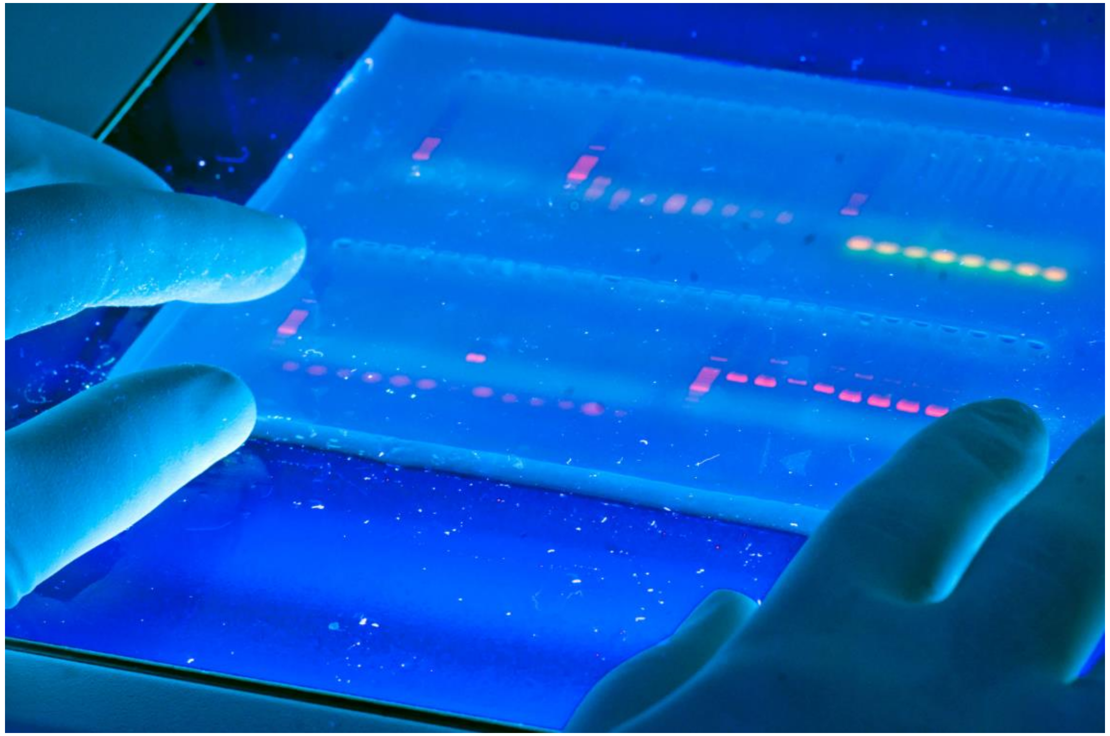
https://www.elveflow.com/microfluidic-reviews/general-microfluidics/materials-for-microfluidic-chips-fabrication-a-review-2017/

Outros materiais

Papel



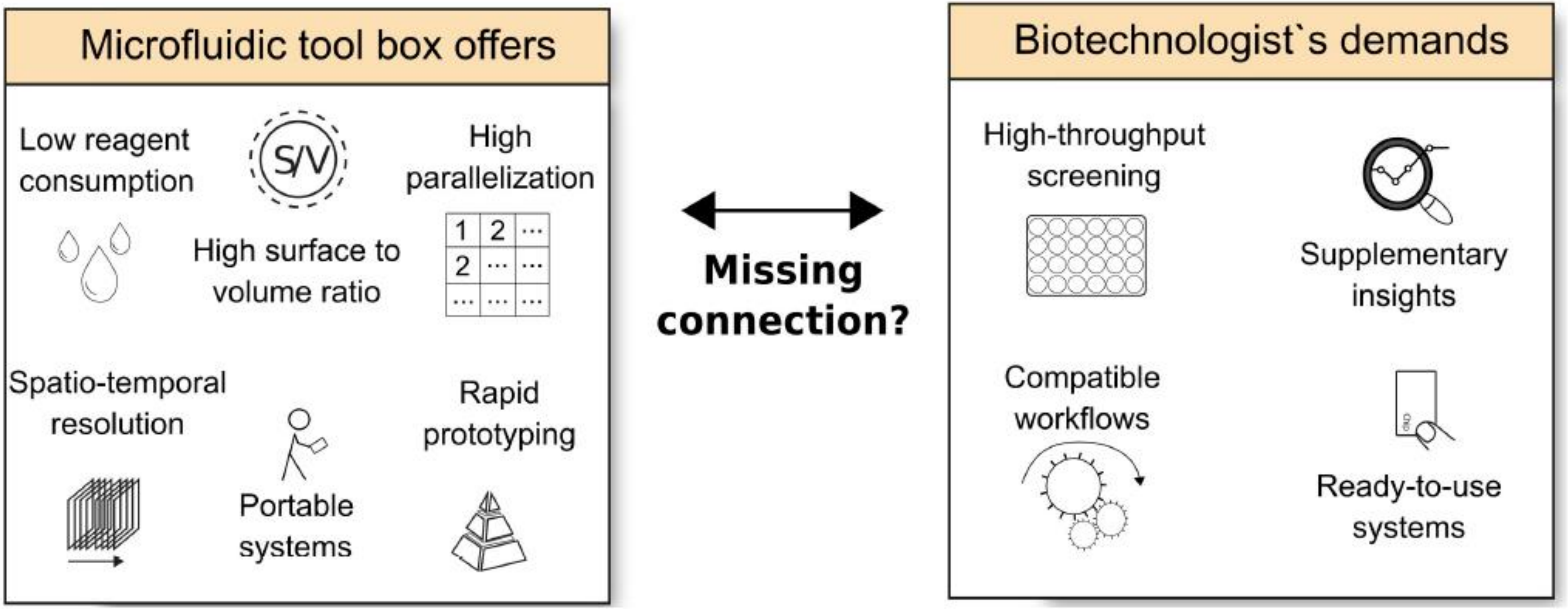
Hidrogéis



https://www.elveflow.com/microfluidic-reviews/general-microfluidics/materials-for-microfluidic-chips-fabrication-a-review-2017/

ENGENHARIA DE MICROSSISTEMAS
POSSIBILIDADES

ÁREA BIOTECNOLÓGICA
DEMANDAS



Ortseifen et al. 2020

Exemplos de aplicação em microfluídica

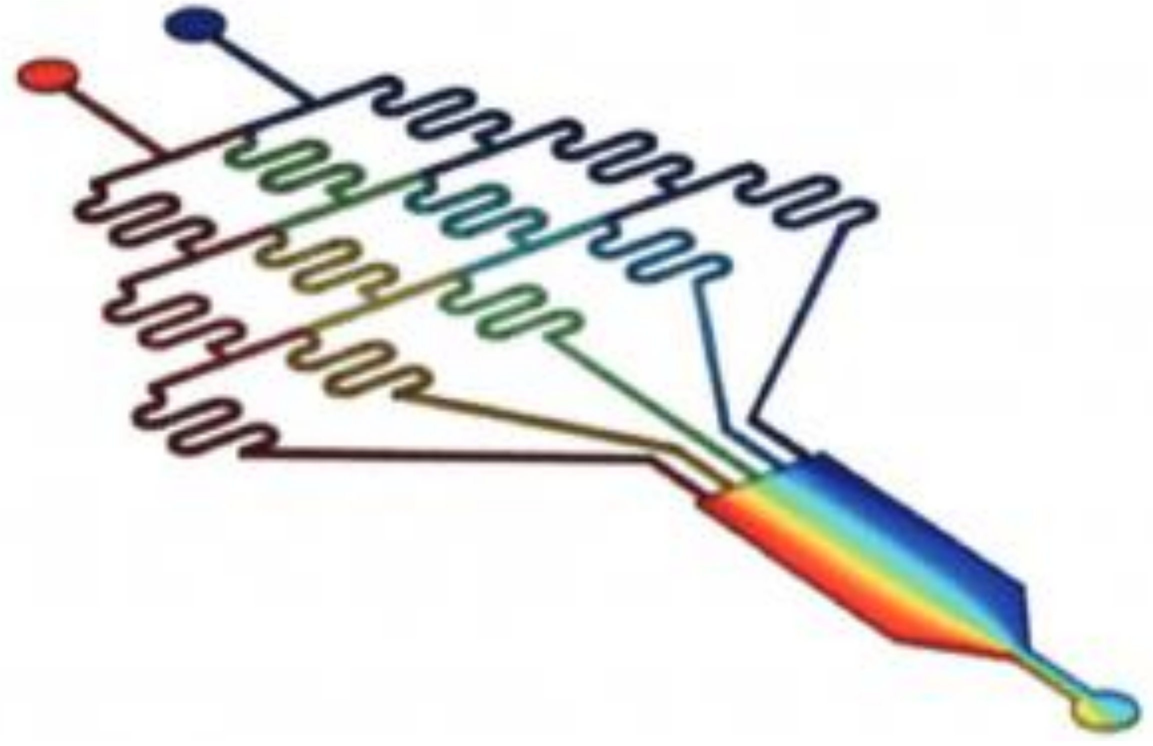
- In vitro dynamic models
- Point of care applications
- Cell behavior
- Synthesis of Nano and Biomaterials
- Drug screening
- Síntese de nanopartículas
- Síntese de microgéis

Microfluídica & Células

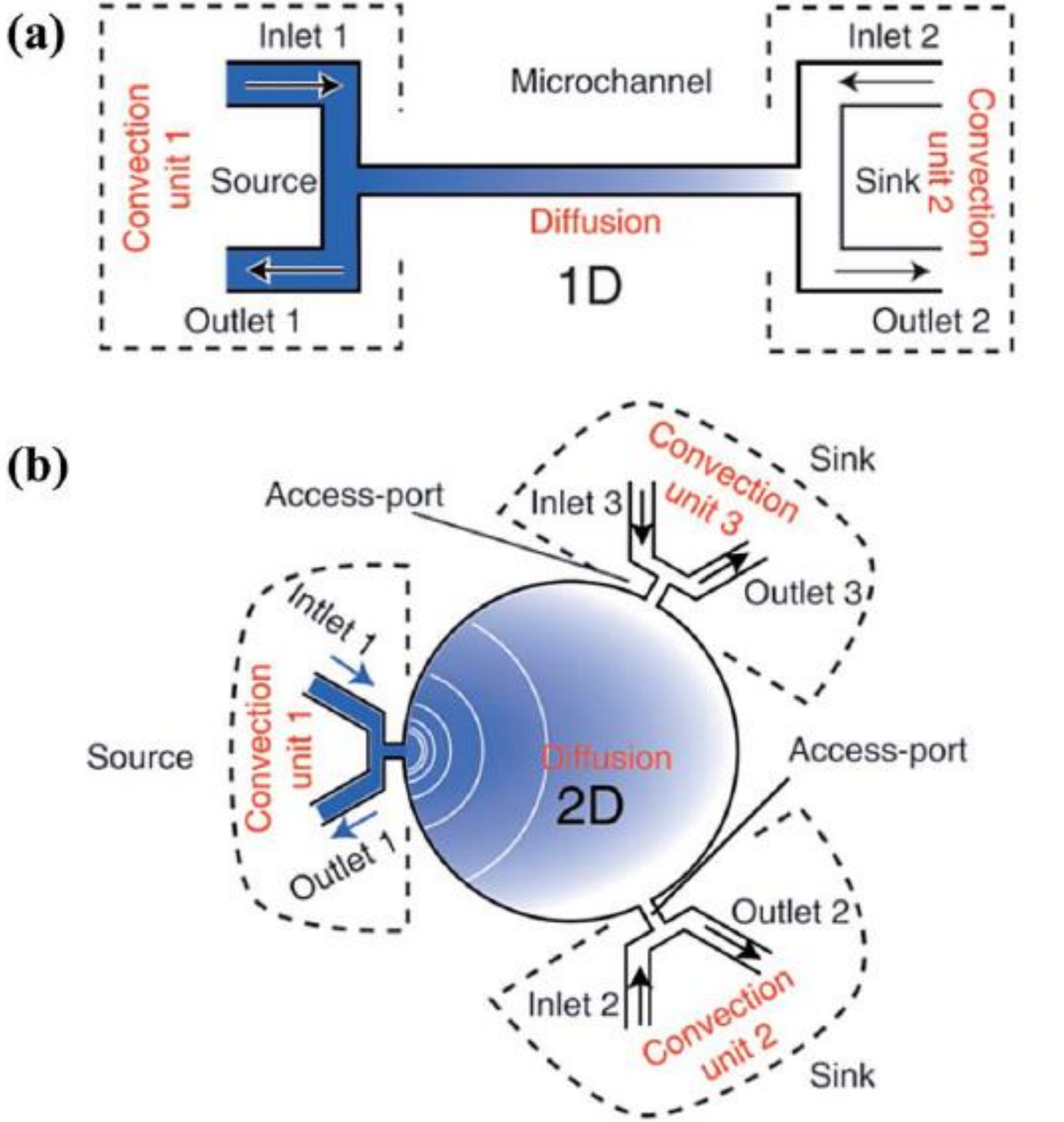
Gradientes de concentração

Difusivo

Convectivo

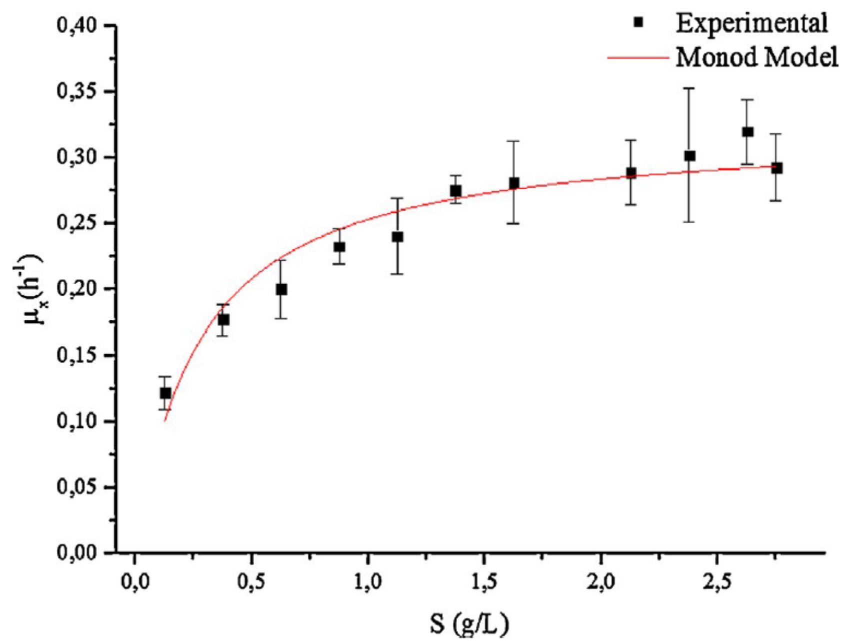


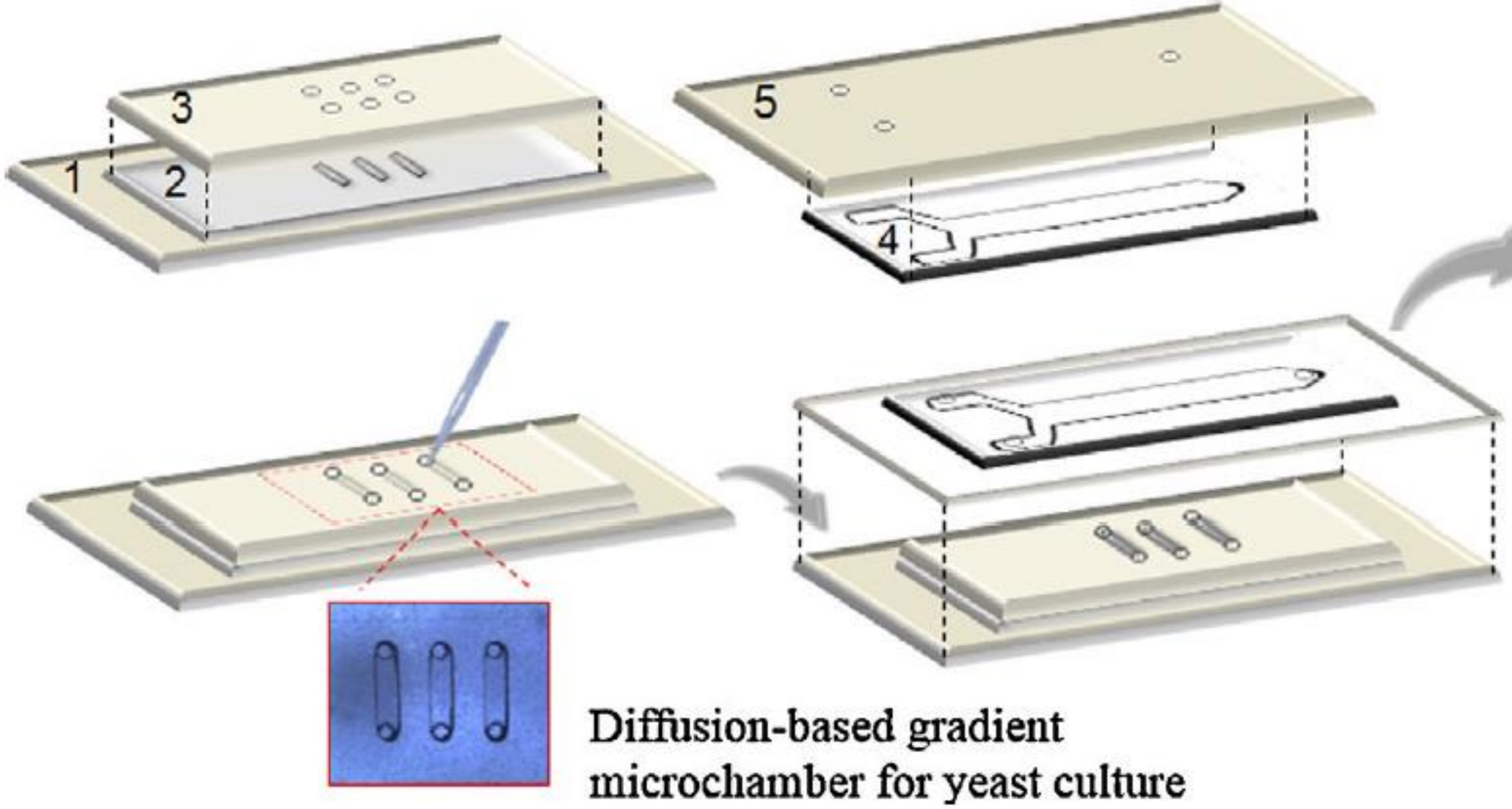
https://www.elveflow.com/microfluidics-research-horizon-europe/beta-innovation/microfluidics-pilot-packs/concentration-gradient-pilot-pack/

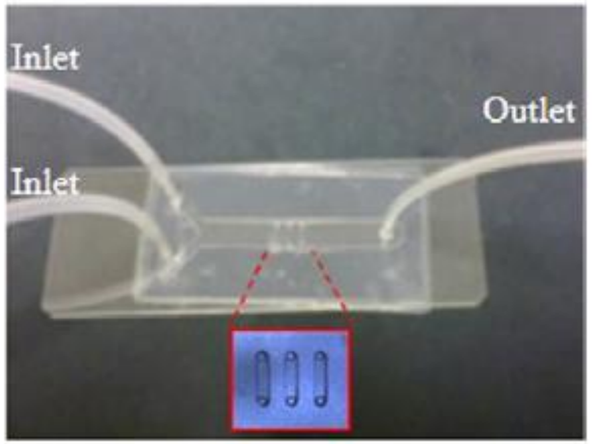


J. Atencia, G. A. Cooksey and L. E. Locascio, A robust diffusion-based gradient generator for dynamic cell assays, *Lab Chip*, 2012, **12**(2), 309–316.

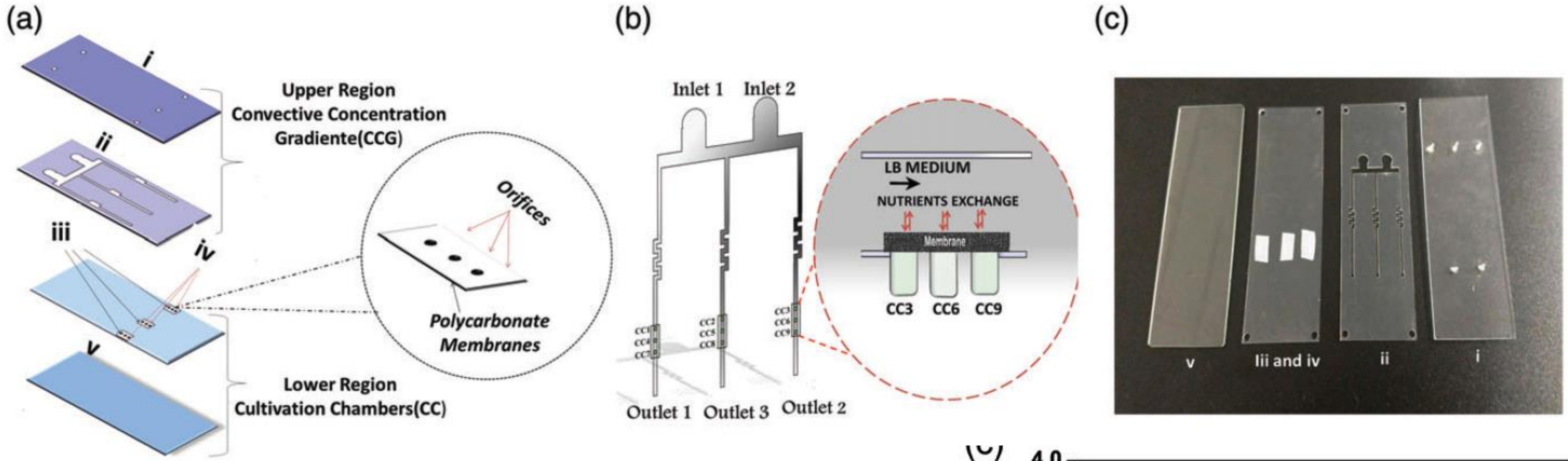
Gradiente de concentração difusivo
Saccaromyces cereviseae



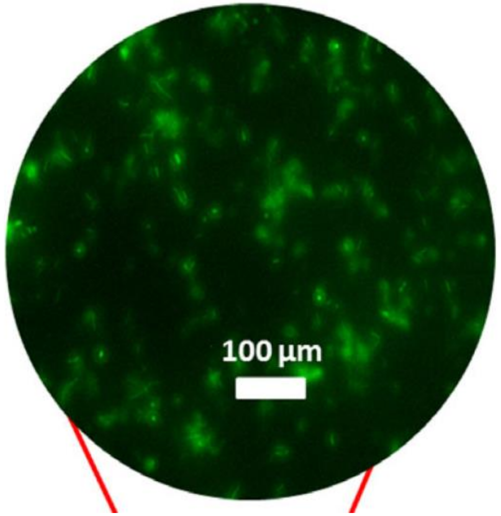


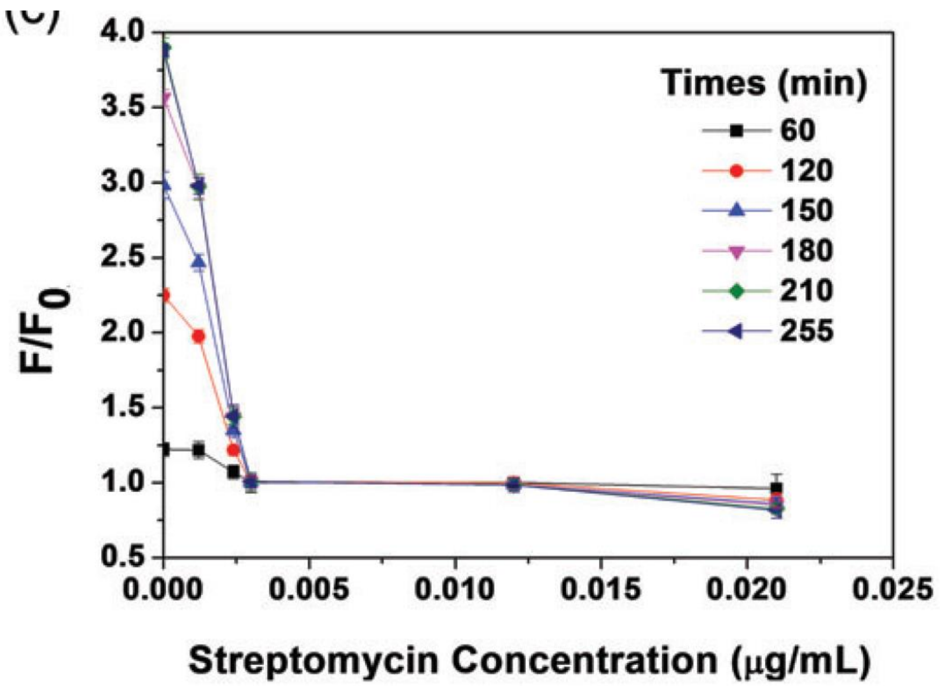


Oliveira et al., Biochemical Eng, 2015



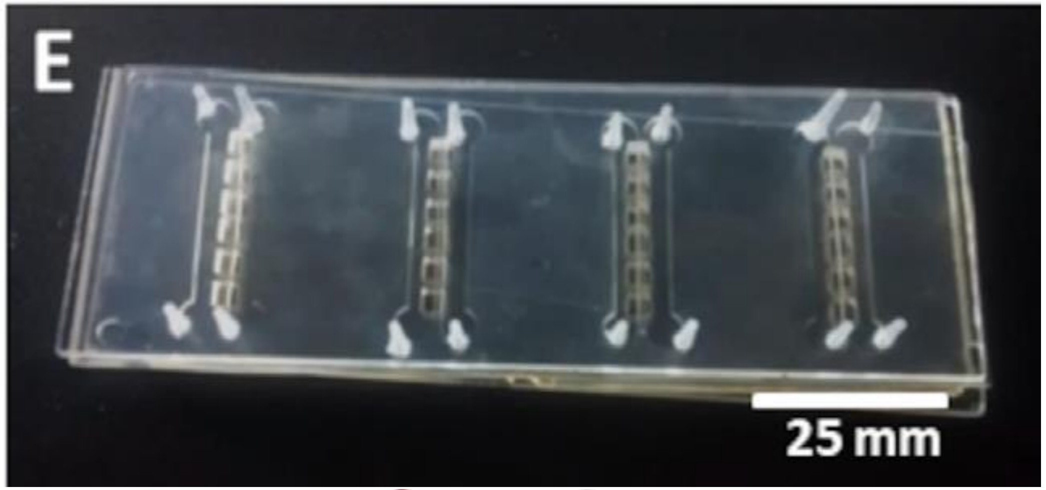
Gradiente de concentração convectivo *Eschericihia coli*

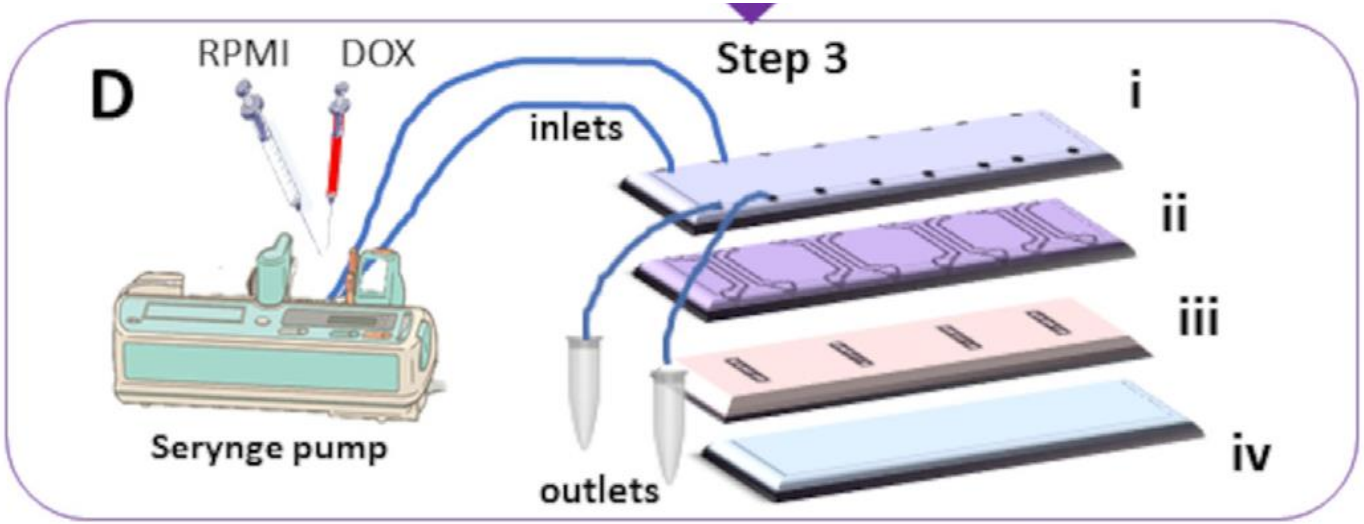


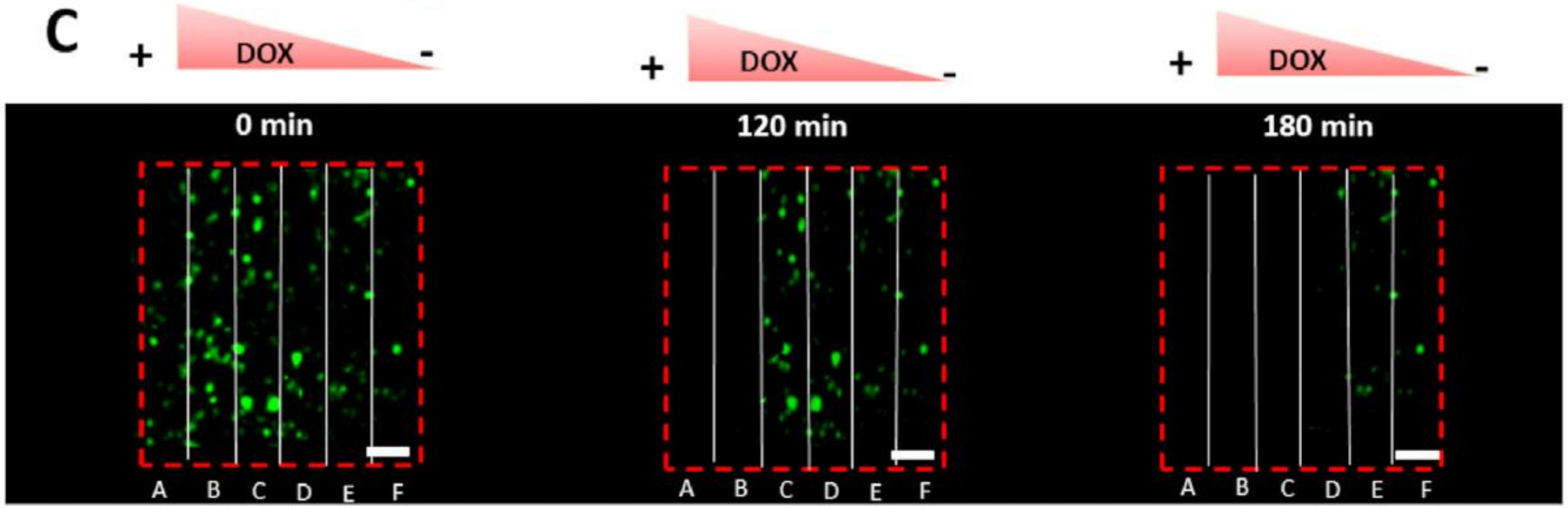


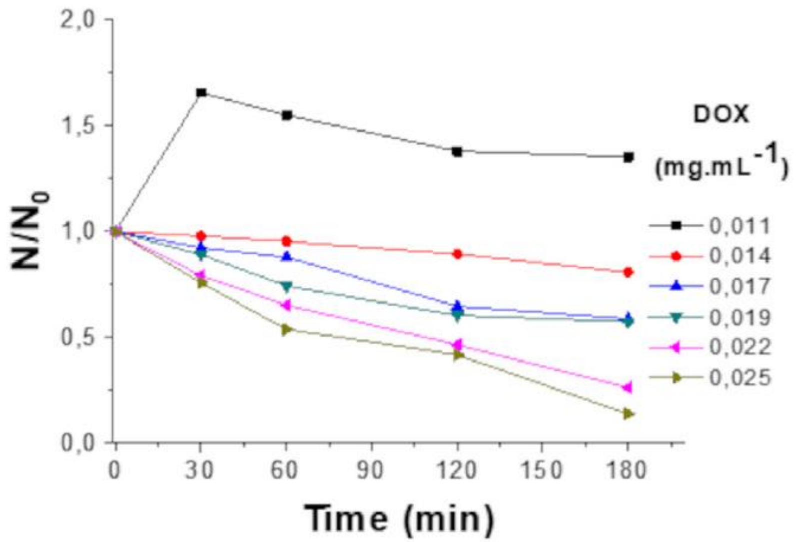
Vit et al. 2018

Gradiente de concentração difusivo - Células de câncer de mama – MCF-7







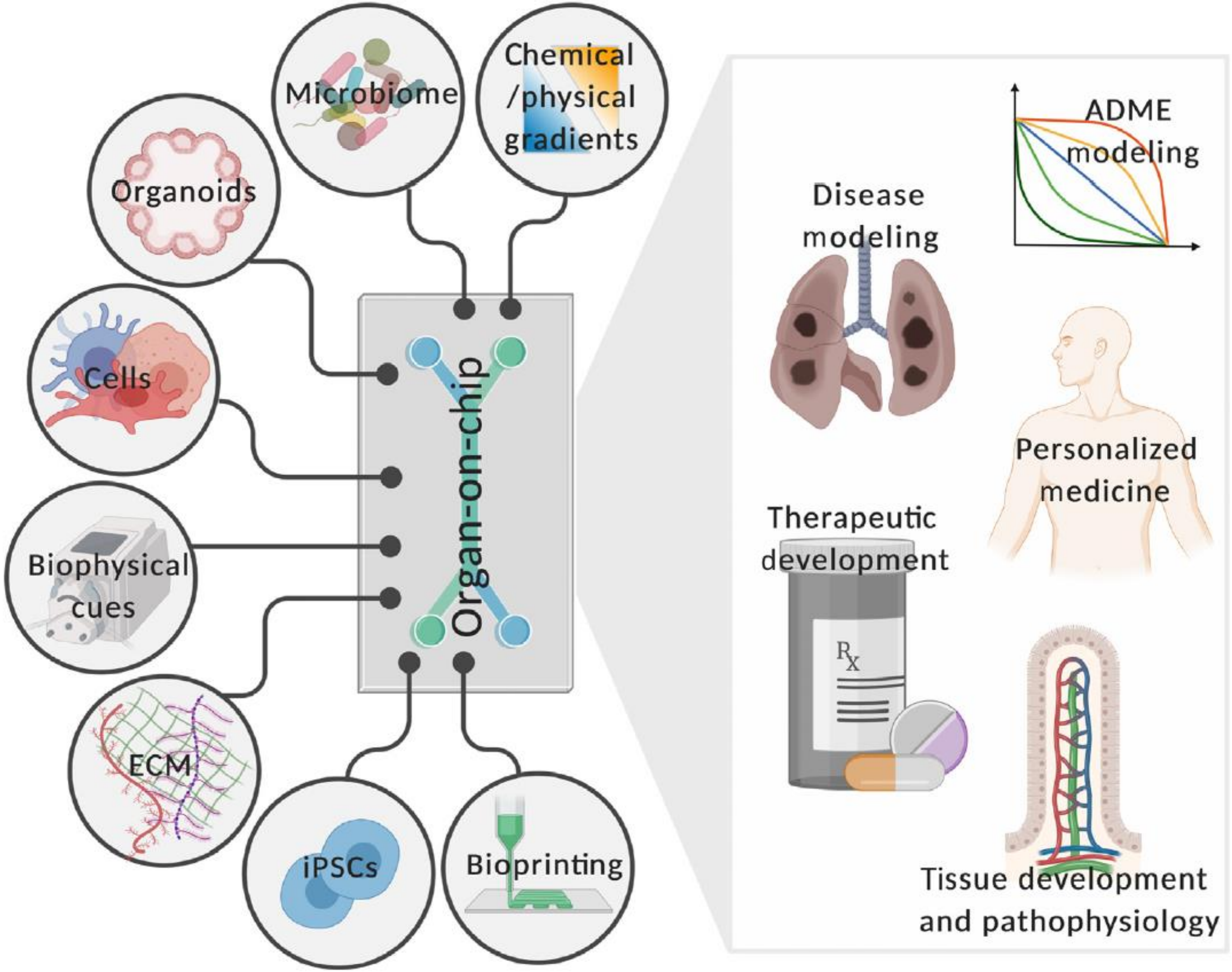


Vit et al., Analytica Chimica Acta, 2021

Organ on a chip

Versus

Body on a chip



Jalili-Firoozinezhad et al., 2021

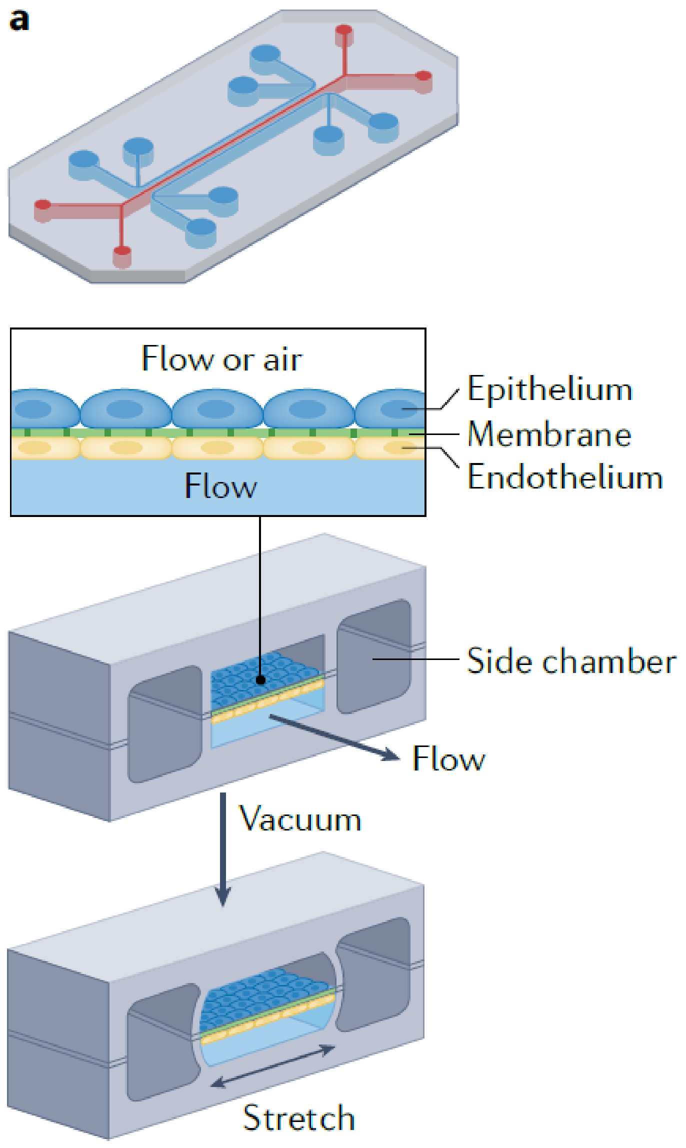
Sistemas que mimetizam a microfisiologia de tecidos

Engenharia de microsistemas
Engenharia de tecidos
Microbiologia cellular

Reconstituição de órgãos e tecidos

Sistemas 3D estáticos e grande complexidade

Sistemas com escoamento de fluidos (organ-on-a-chip)



Ingber, Nature Reviews, 2022

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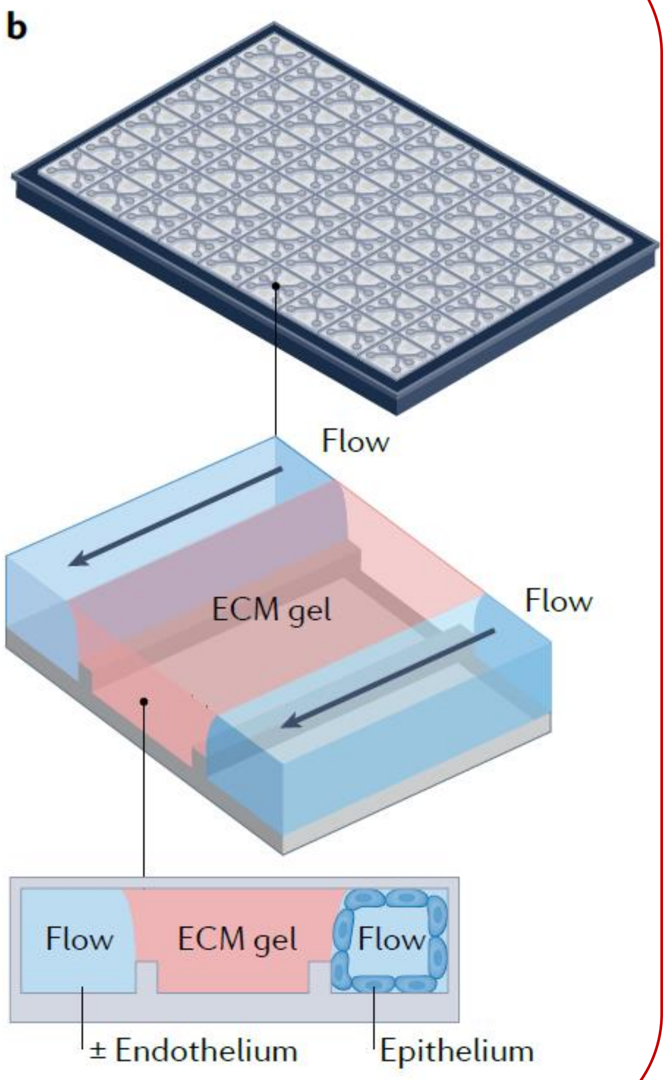
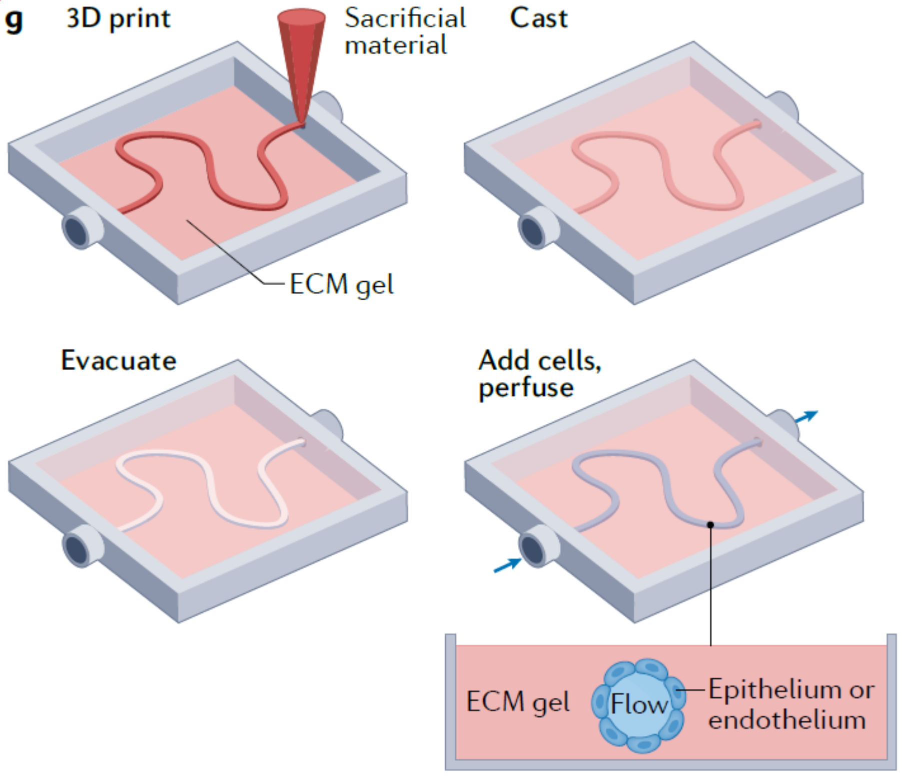
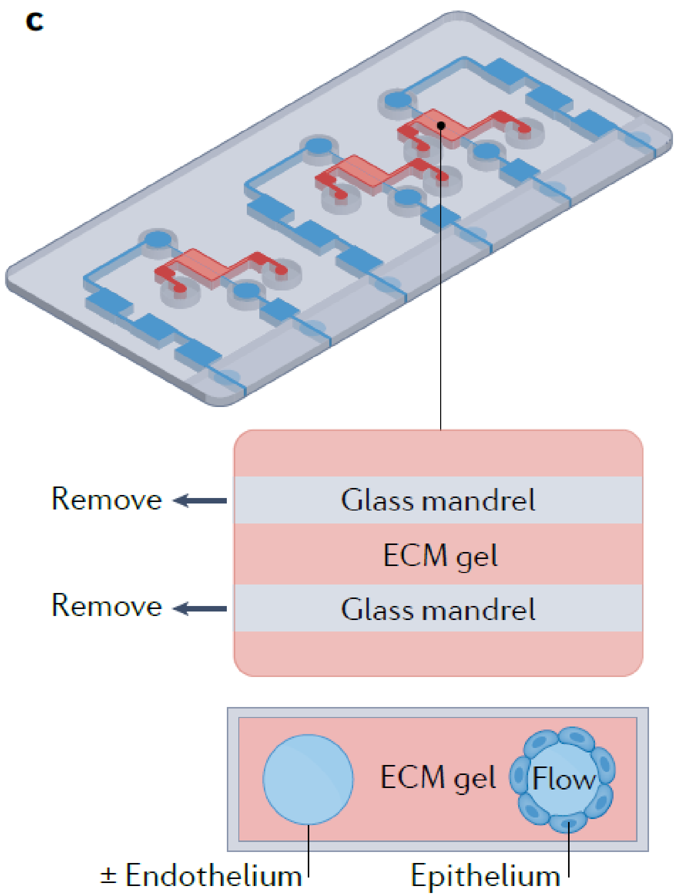
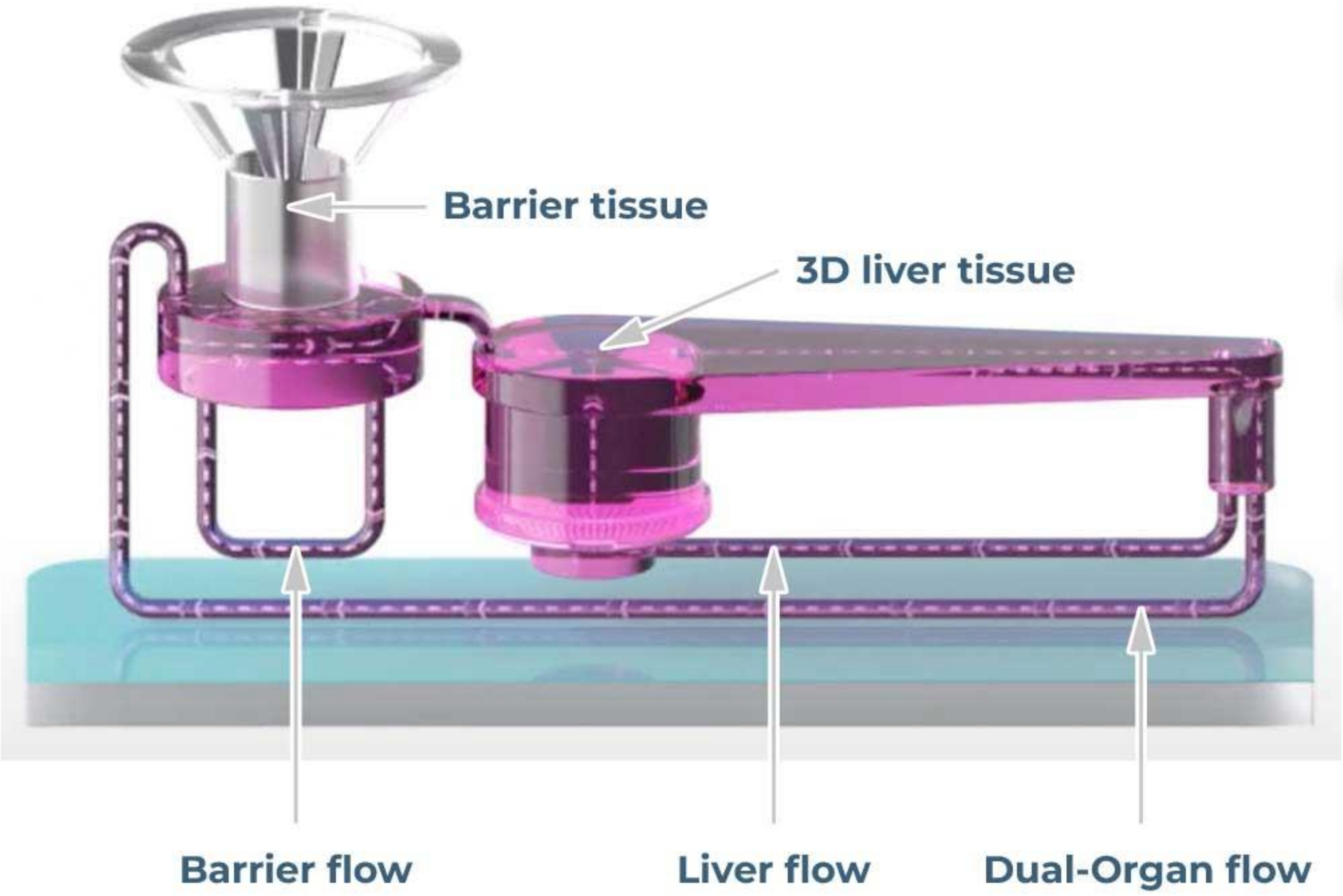


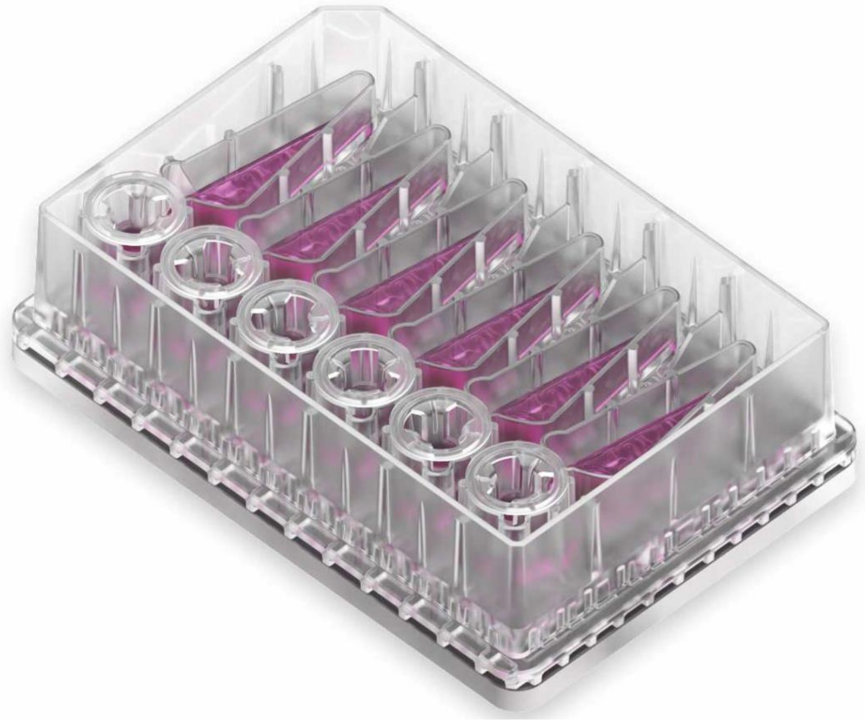




Ingber, Nature Reviews, 2022

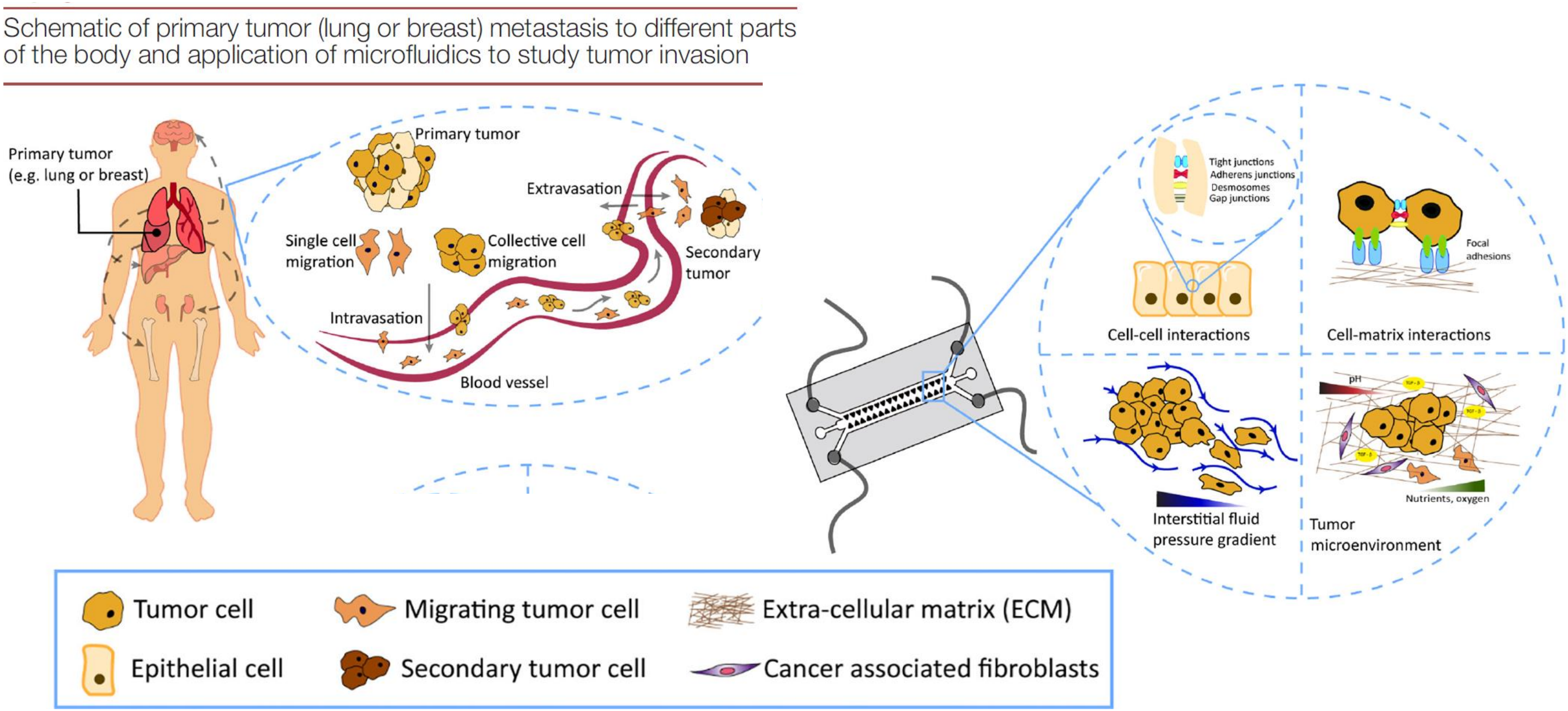
Sistemas que mimetizam a microfisiologia de tecidos





https://cn-bio.com/consumables/multi-chip-plates/physiomimix-dual-organ-plate/

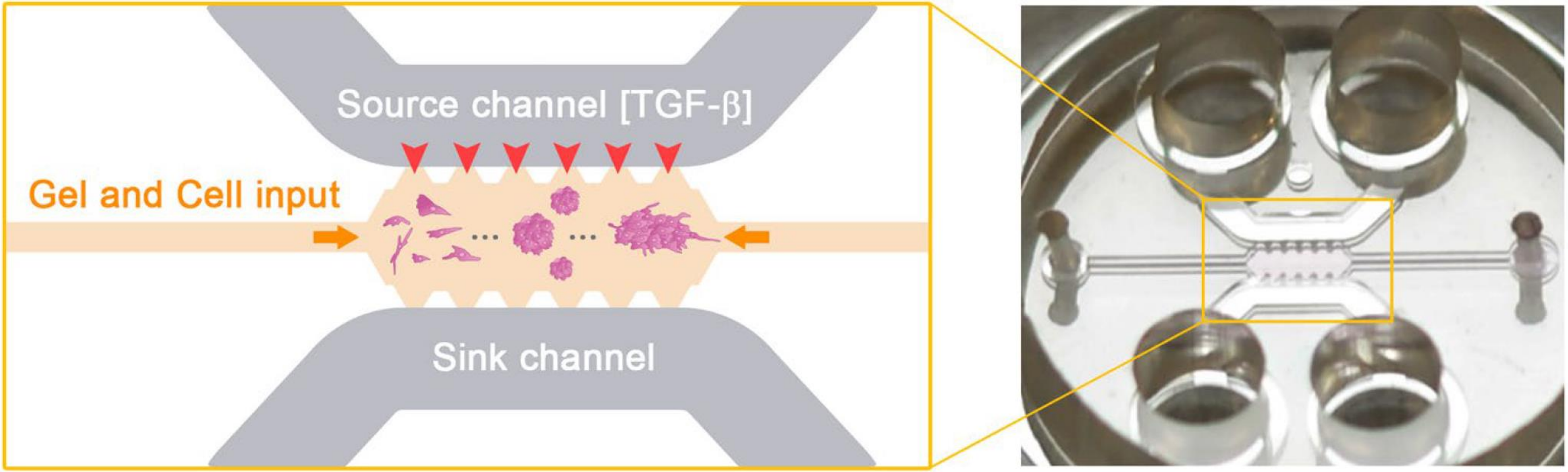
Microfluídica associada ao estudo da migração de células em cultivo 3D



Mehta et al. Trends in Cancer. 2022

From individual to collective 3D cancer dissemination: roles of collagen concentration and TGF-β

J. Plou, Y. Juste-Lanas, V. Olivares, C. del Amo, C. Borau & J. M. García-Aznar

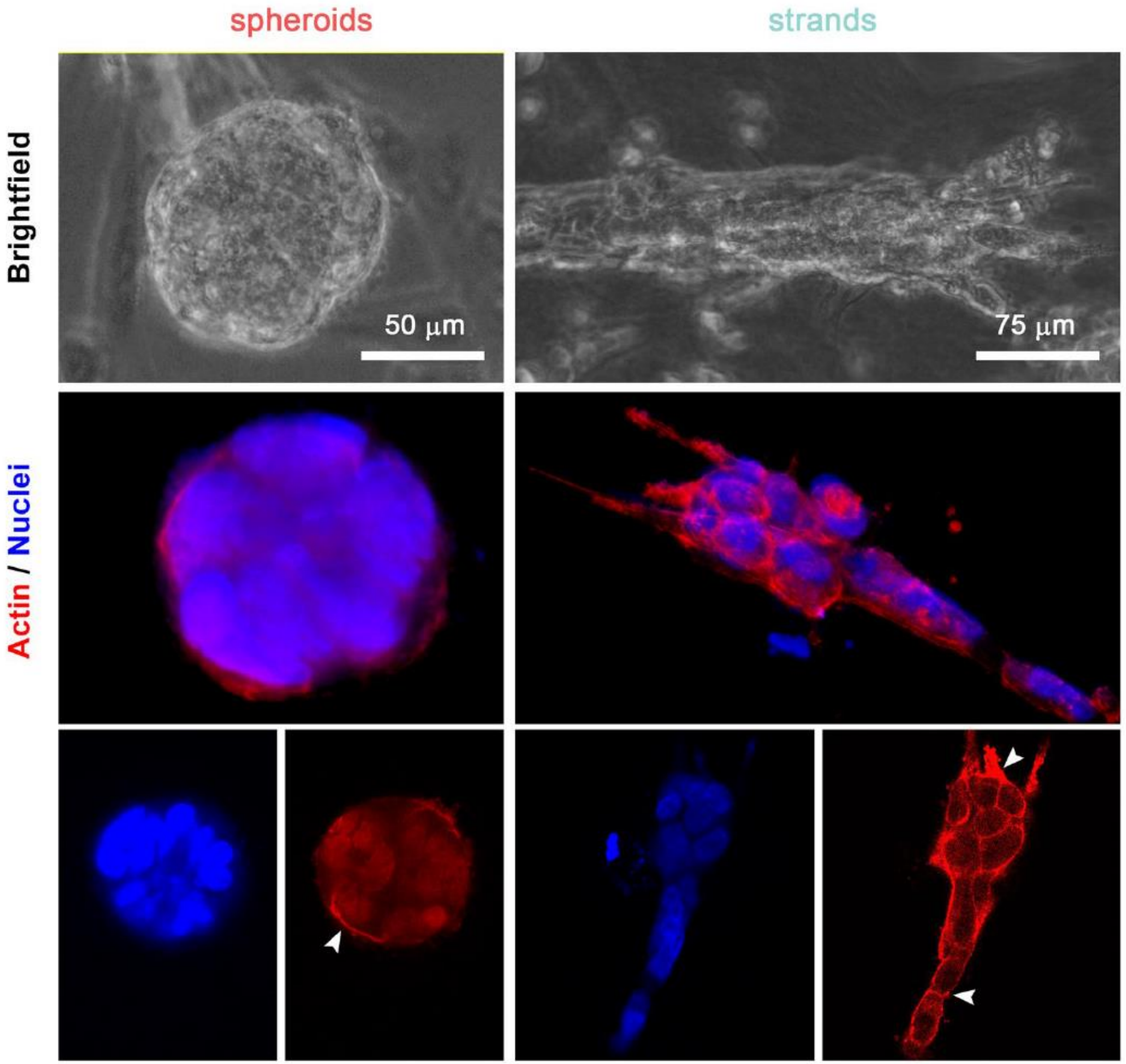


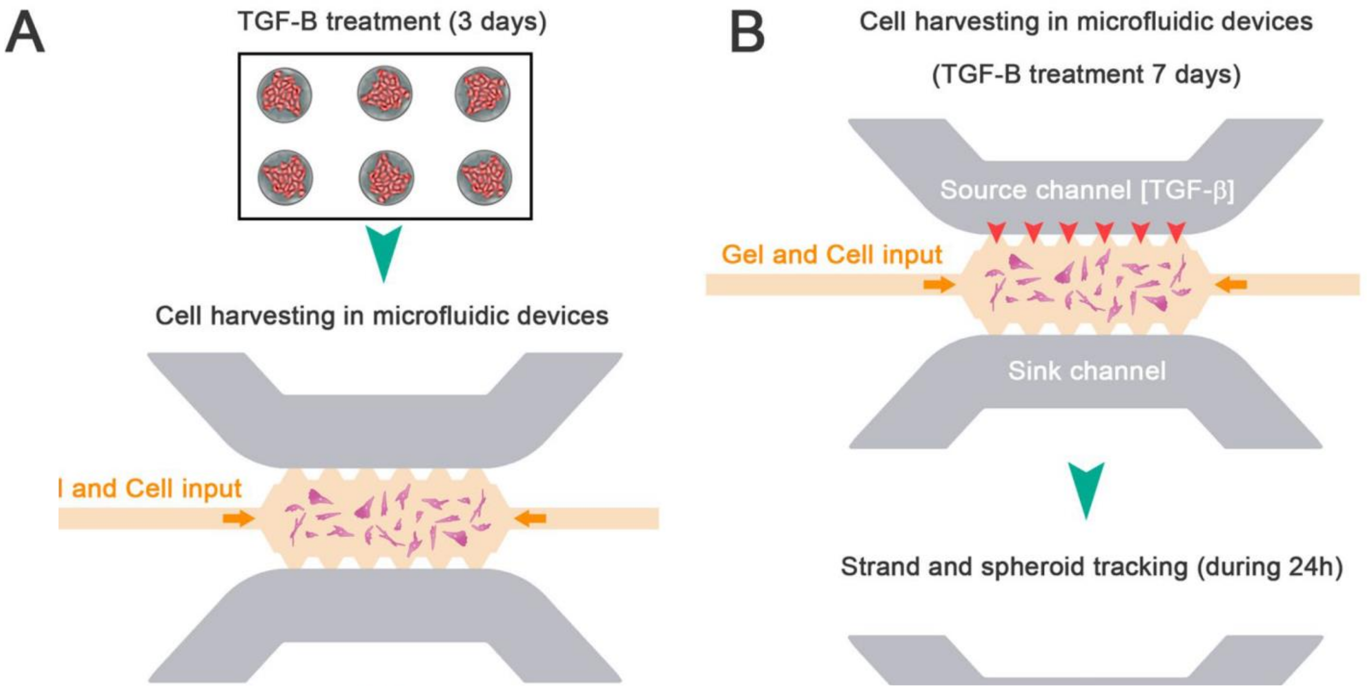
H1299 cell (a non-small cell lung cancer cell line)

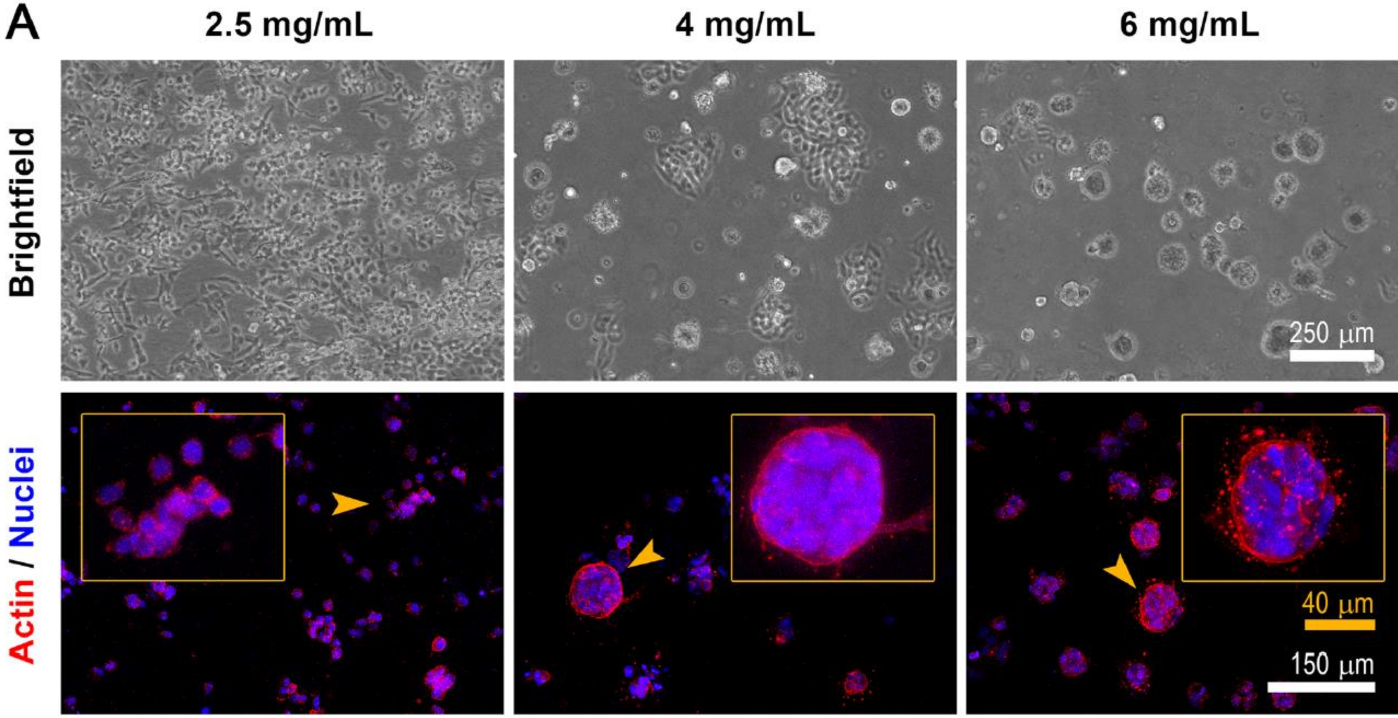
Plou et al., 2018

From individual to collective 3D cancer dissemination: roles of collagen concentration and TGF-β

J. Plou, Y. Juste-Lanas, V. Olivares, C. del Amo, C. Borau & J. M. García-Aznar







Mimetizando a arquitetura do tecido – o caso da barreira hemato encefálica

Modelo Real

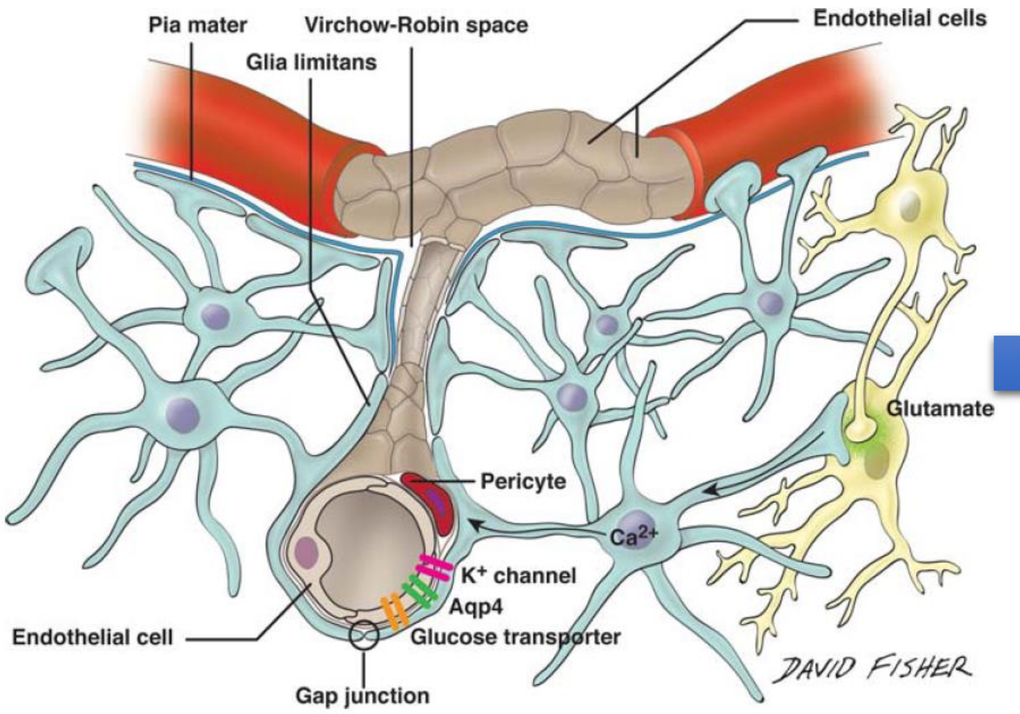
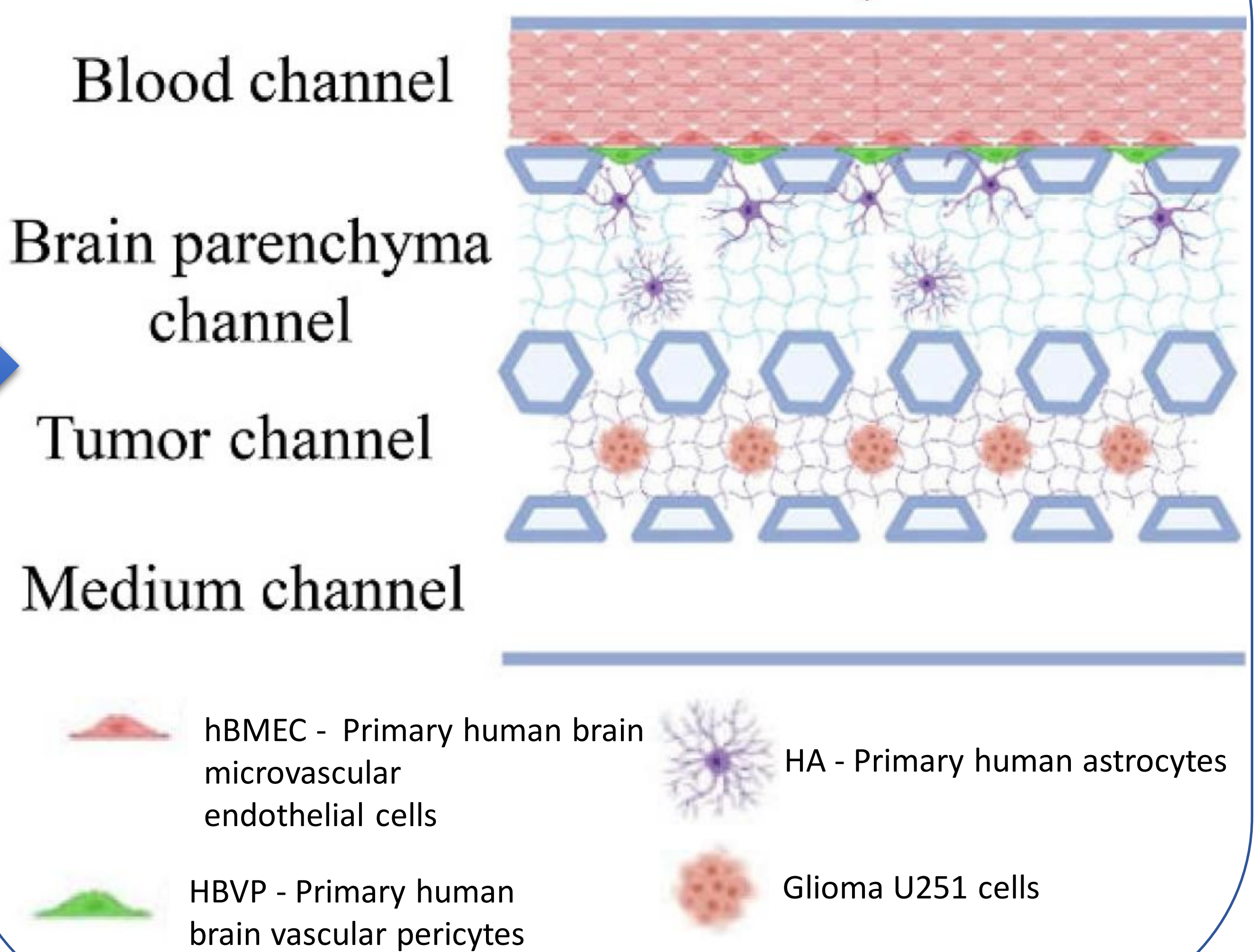


Fig. 1. Schematic drawing of the blood brain barrier. Note the glia limitans and Virchow-Robin spaces. [Color figure can be viewed at wileyonlinelibrary.com]

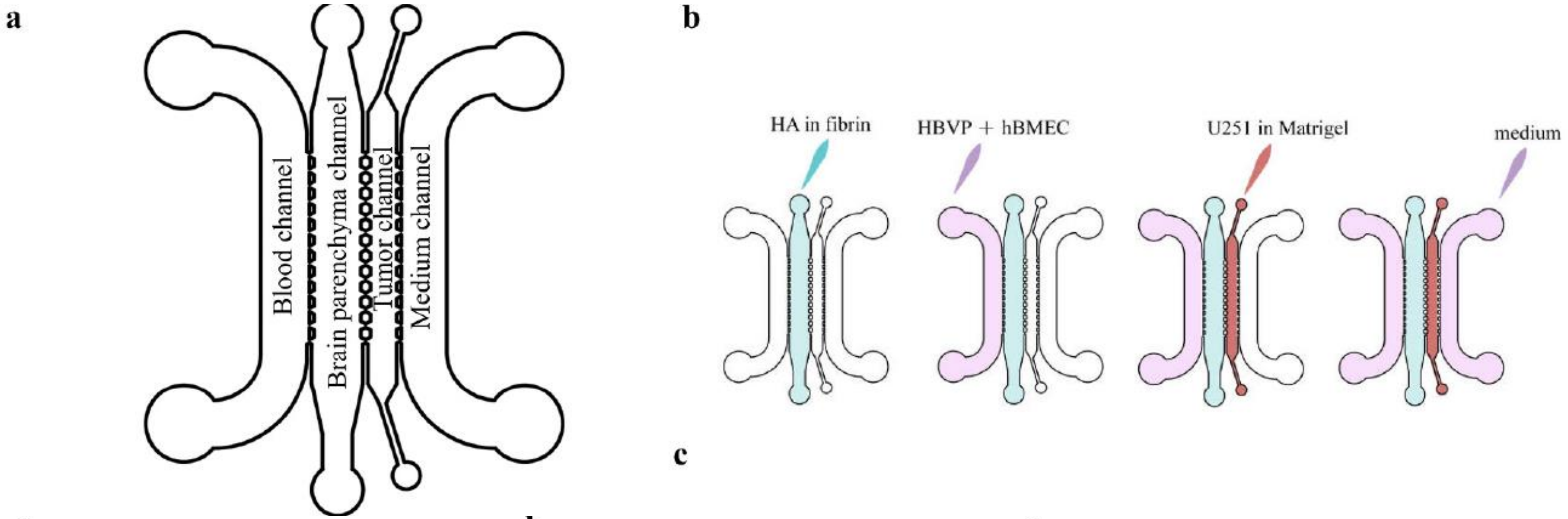
Sharif et al., 2018

Modelo de Engenharia

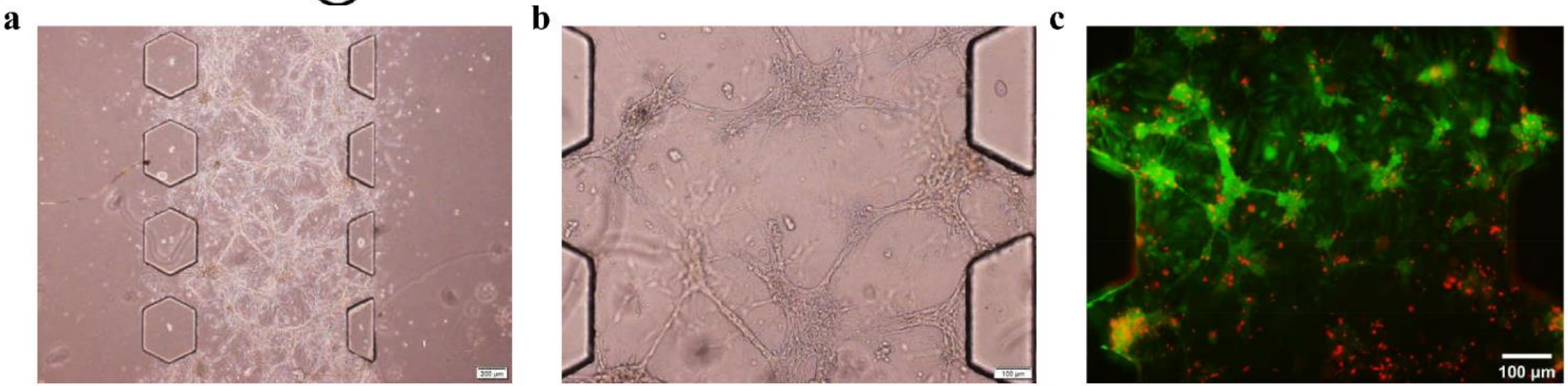


Shi et al. 2023

Barreira Hemato Encefálica



Glioma cells

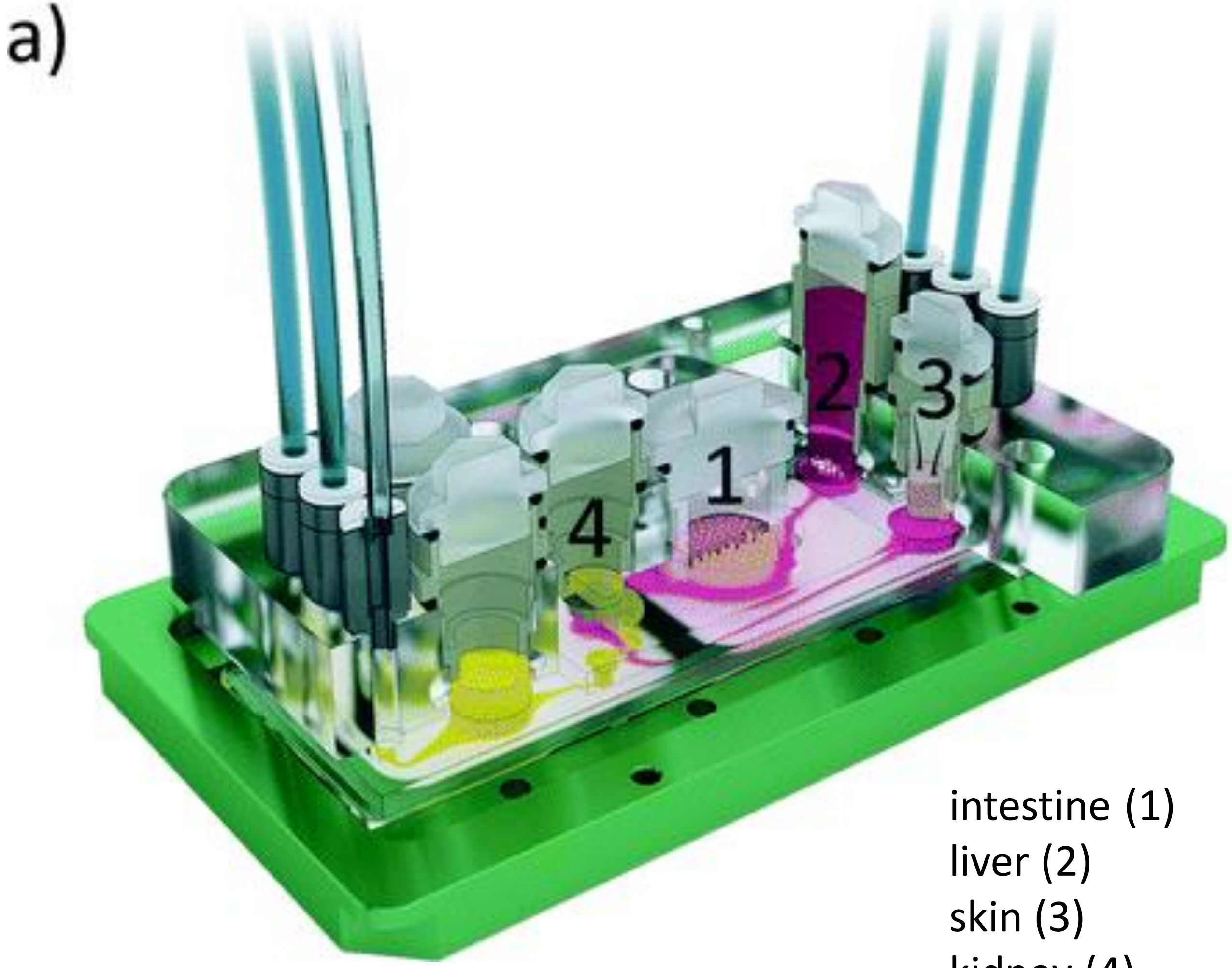


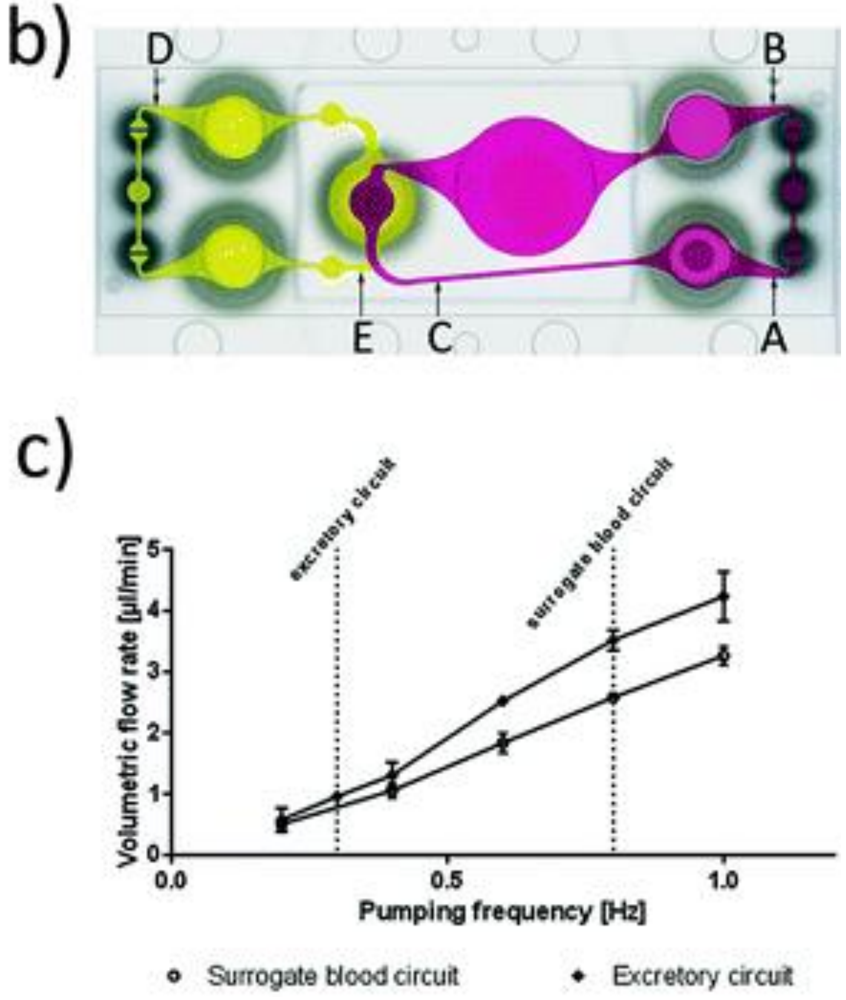
Start test

Fig. 6. Growth of U251 multicellular spheroids on microfluidic chip. (A–B) Brightfield image of U251 multicellular spheroids on microfluidic chip; (C) Live/Dead staining of U251 multicellular spheroids on microfluidic chip.

Shi et al. 2023

Body on a chip





intestine (1)
liver (2)
skin (3)
kidney (4)

Ilka Maschmeyer et al., 2015

Modelos de estudo e sua relevância fisiológica

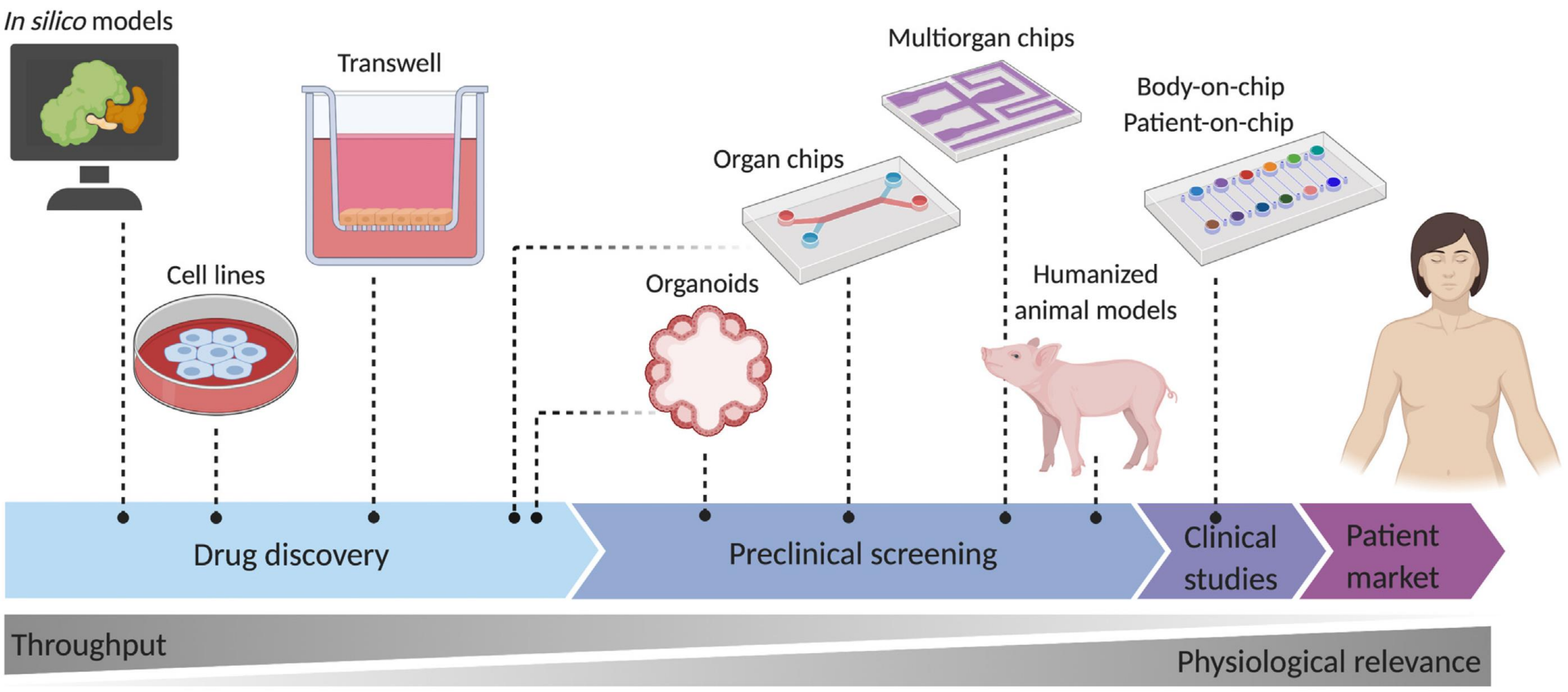
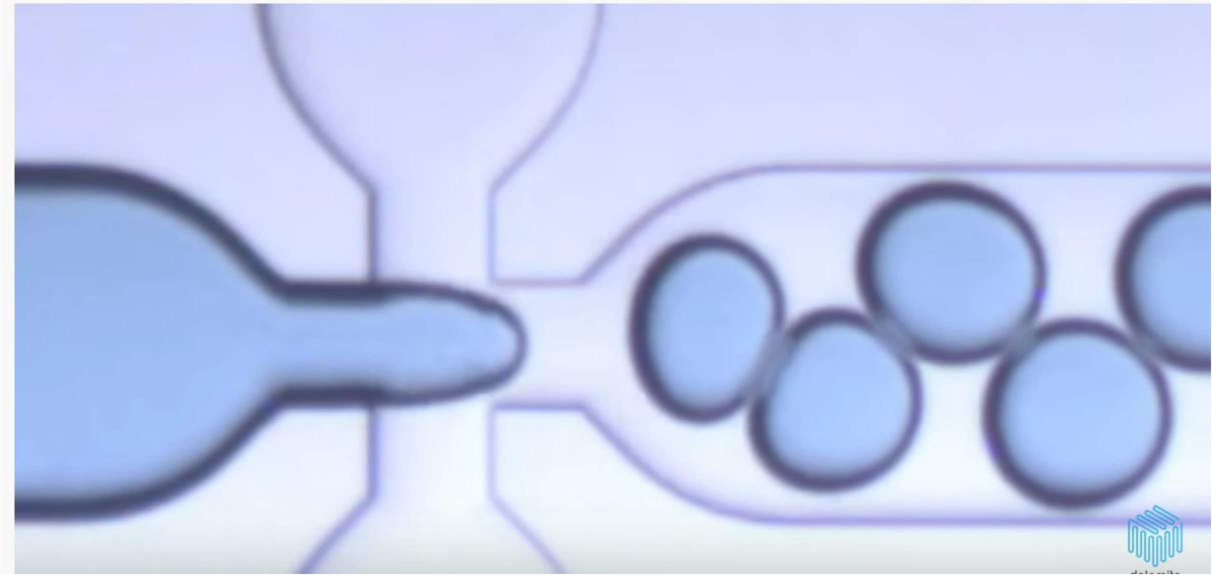


Figure 5. Comparison of Model Throughput versus Physiological Relevance of *In Vitro* Tissue Culture Platforms. *In vitro* technologies have certain roles at different stages of the drug development process. 2D and *in silico* models enable rapid and high-throughput drug screening and disease modeling; however, they lack the 3D physiological tissue microenvironment and fail to recapitulate complex organ-level responses, disease phenotypes, and pharmacokinetic (PK)/pharmacodynamic (PD) behavior *in vitro*. By contrast, multiorgan-on-chip systems offer better mimicry of human physiology and pathophysiology, although at a lower physiological relevance than animal models. While the scaling up and maintenance of body- or autologous patient-on-chip technology are sometimes more challenging than the creation of humanized animal models, they can enable personalized precision medicine approaches and clinical trials in the laboratory. Created with BioRender.com.

Jalili-Firoozinezhad et al., Trends in Biotechnlogy/Cell Press, 2021

Microfluídica de Gotas



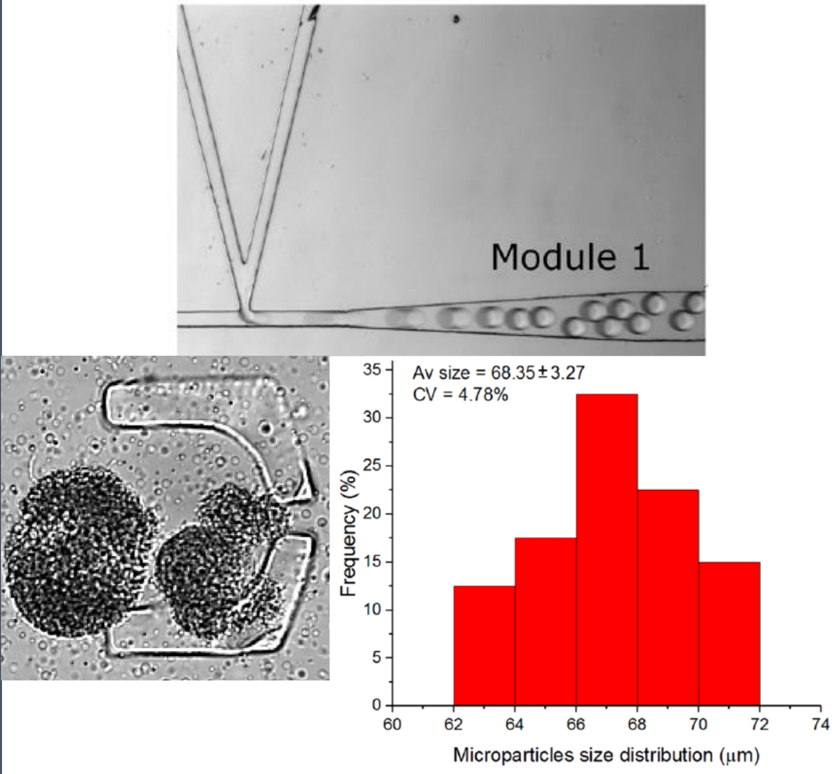
https://www.youtube.com/watch?v=EjyM8sNplm4

Contrastes químicos e físicos:

- Grandes diferenças nas propriedades dos líquidos “externo” e “interno” da gota (fases contínua e dispersa, respectivamente);
  - Constante dielétrica
  - Tensão interfacial
- Interface é deformável!!!

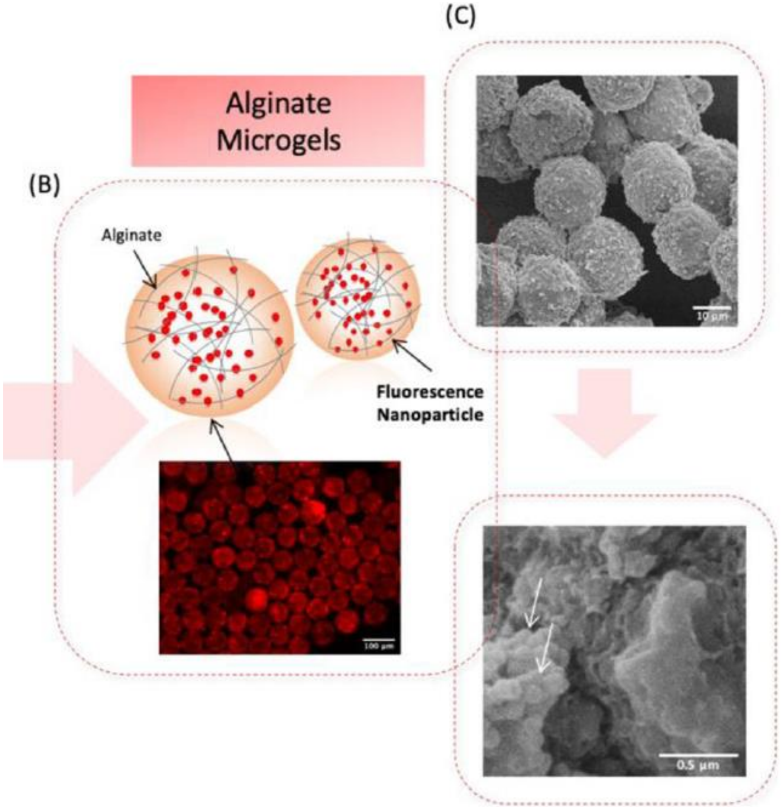
Microfluídica de Gotas

Bacteria encapsulation
biocatalyst



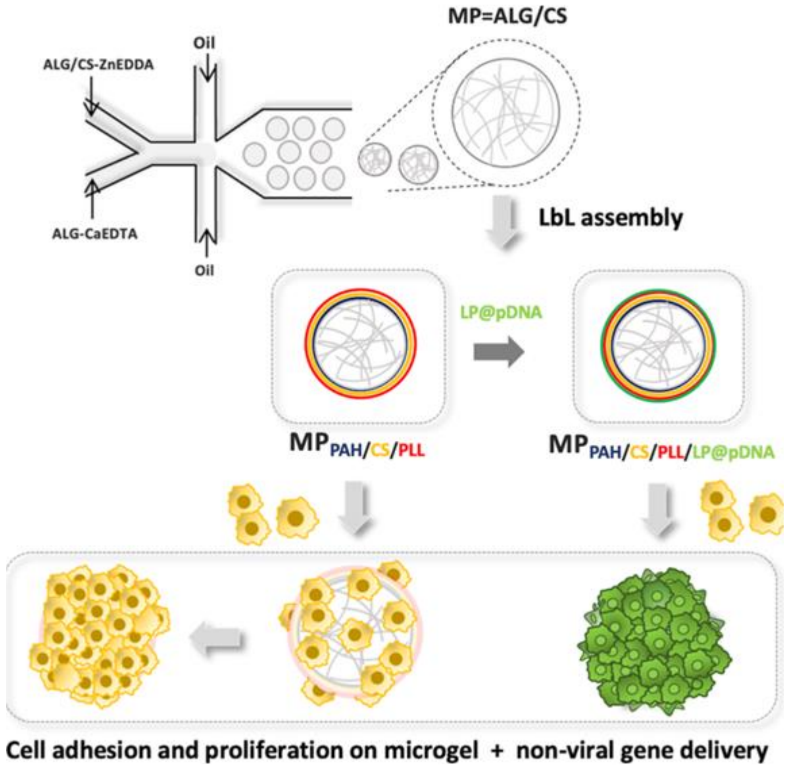
Oliveira et al., Biochemical Eng, 2019
Oliveira et al., Enzyme and Microbial Tech, 2022

Nanoparticle encapsulation
Drug delivery



De Carvalho et al., Materials Science & Engineering C, 2021

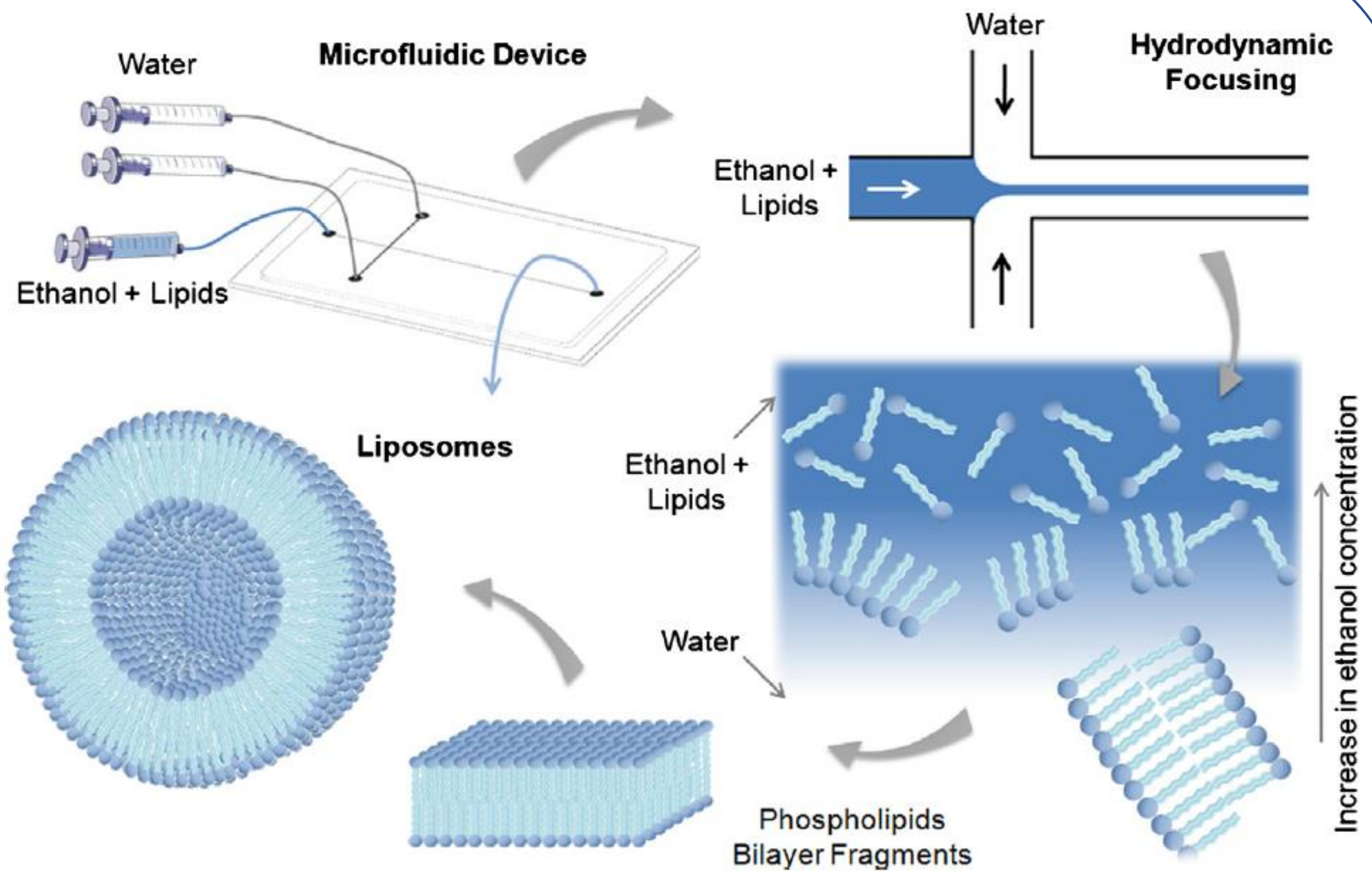
3D Cell Culture and
Nonviral Gene Delivery

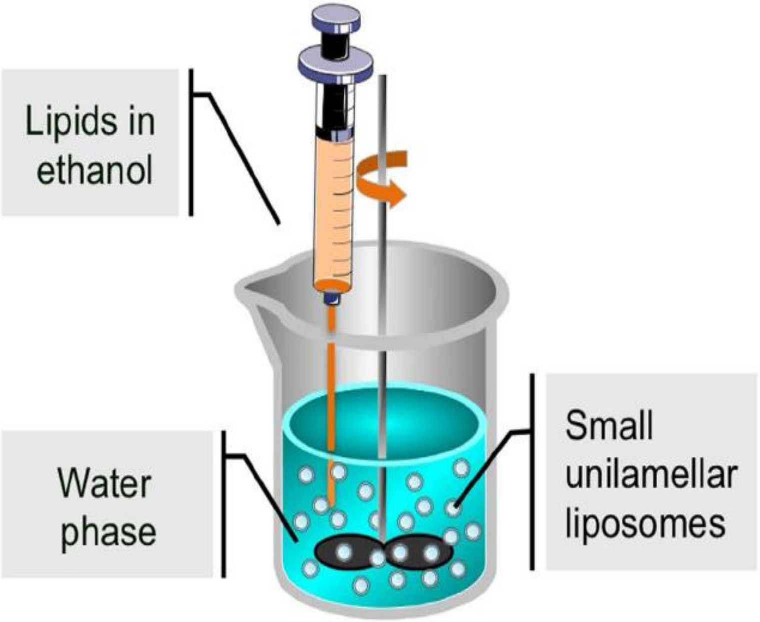


Carvalho et al., Biomacromolecules, 2021

Microfluídica & Nanotecnologia

Flow Focusing Microfluidic Process – Liposome Synthesis





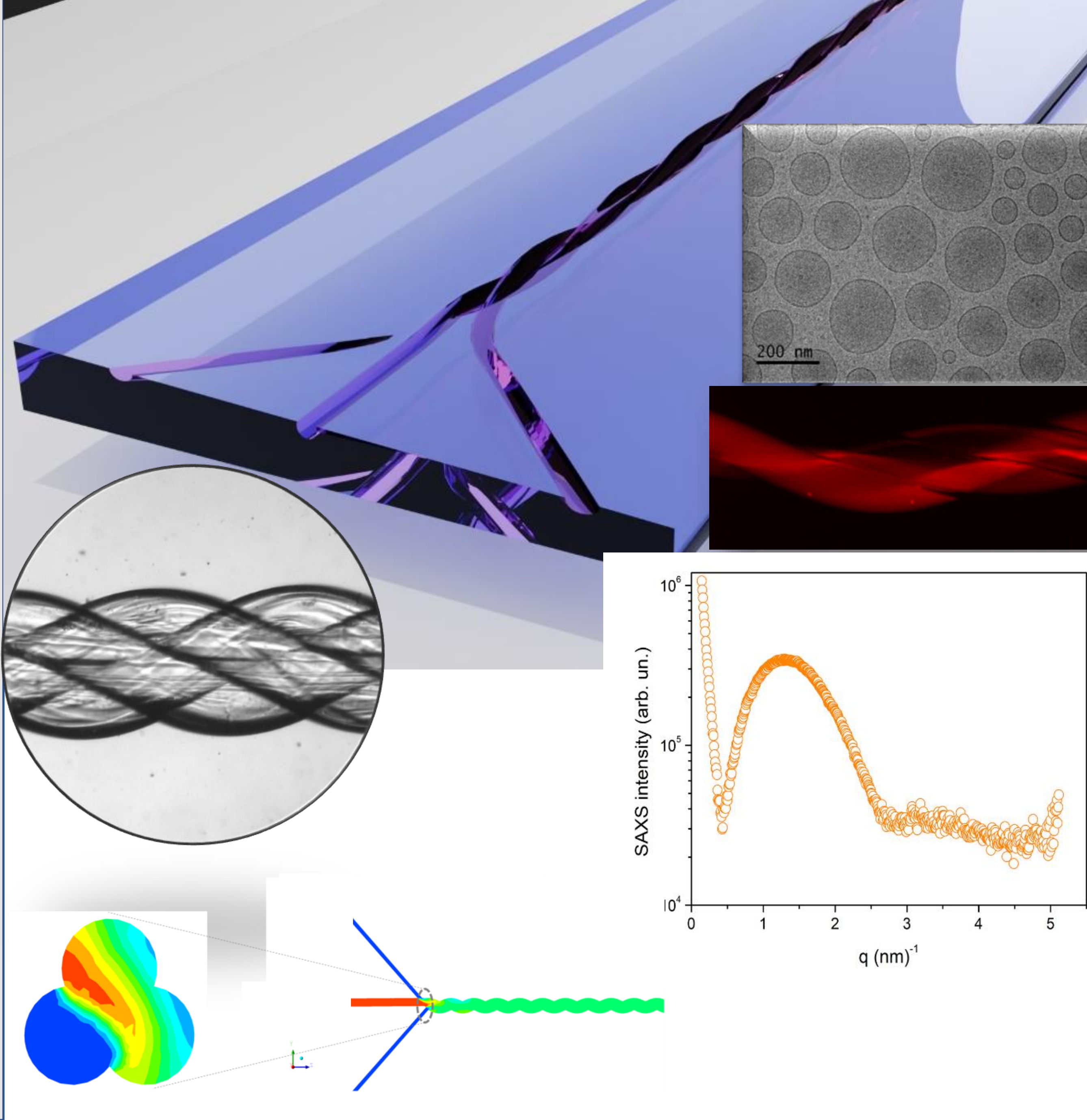
Carugo et al., 2016

Balbino et al. Chem. Eng. J., 2013

Advecção caótica

Síntese de lipossomas
Aumento de produtividade

Firmino et al., Lab on a Chip, 2017



Considerações finais

Microfluídica pode contribuir:

- Desenvolvimentos de modelos in vitro
- Compreensão do comportamento celular dentro de um microssistema complexo
- Acelerar ensaios pré-clínicos para a descoberta de novos fármacos
- Contribuir para acelerar diagnósticos – medicina personalizada
- Desenvolvimento de microgéis para a entrega de fármacos, nanopartículas e células
- Síntese de nanopartículas e sistemas nanoagregados

O desenvolvimento de um microchip requer:

- Desenvolvimento conjunto de profissionais de diversas áreas
- É uma área completamente interdisciplinar
- Requer automação na aquisição de informações e tratamento de dados
- Muito ainda pode ser desenvolvido

Obrigada!!

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LaNBDA

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