



## **Multi-scale modeling for prediction of distributed cellular properties in response to substrate spatial gradients in a continuously run microreactor**

**Lencastre Fernandes, Rita; Krühne, Ulrich; Nopens, Ingmar; Jensen, Anker Degn; Gernaey, Krist V.**

*Publication date:*  
2012

*Document Version*  
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

*Citation (APA):*

Lencastre Fernandes, R., Krühne, U., Nopens, I., Jensen, A. D., & Gernaey, K. (2012). Multi-scale modeling for prediction of distributed cellular properties in response to substrate spatial gradients in a continuously run microreactor. Poster session presented at 11th International Symposium on Process Systems Engineering, Singapore.

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# Multi-scale modelling for prediction of distributed cellular properties

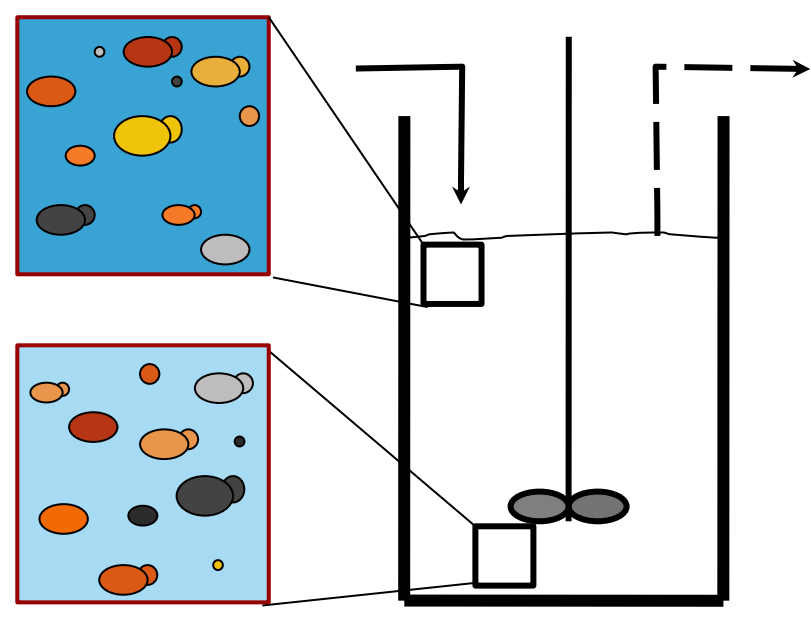


R. Lencastre Fernandes<sup>1</sup>, U. Krühne<sup>1</sup>, I. Nopens<sup>2</sup>, A. D. Jensen<sup>3</sup>, K. V. Gernaey<sup>1</sup>

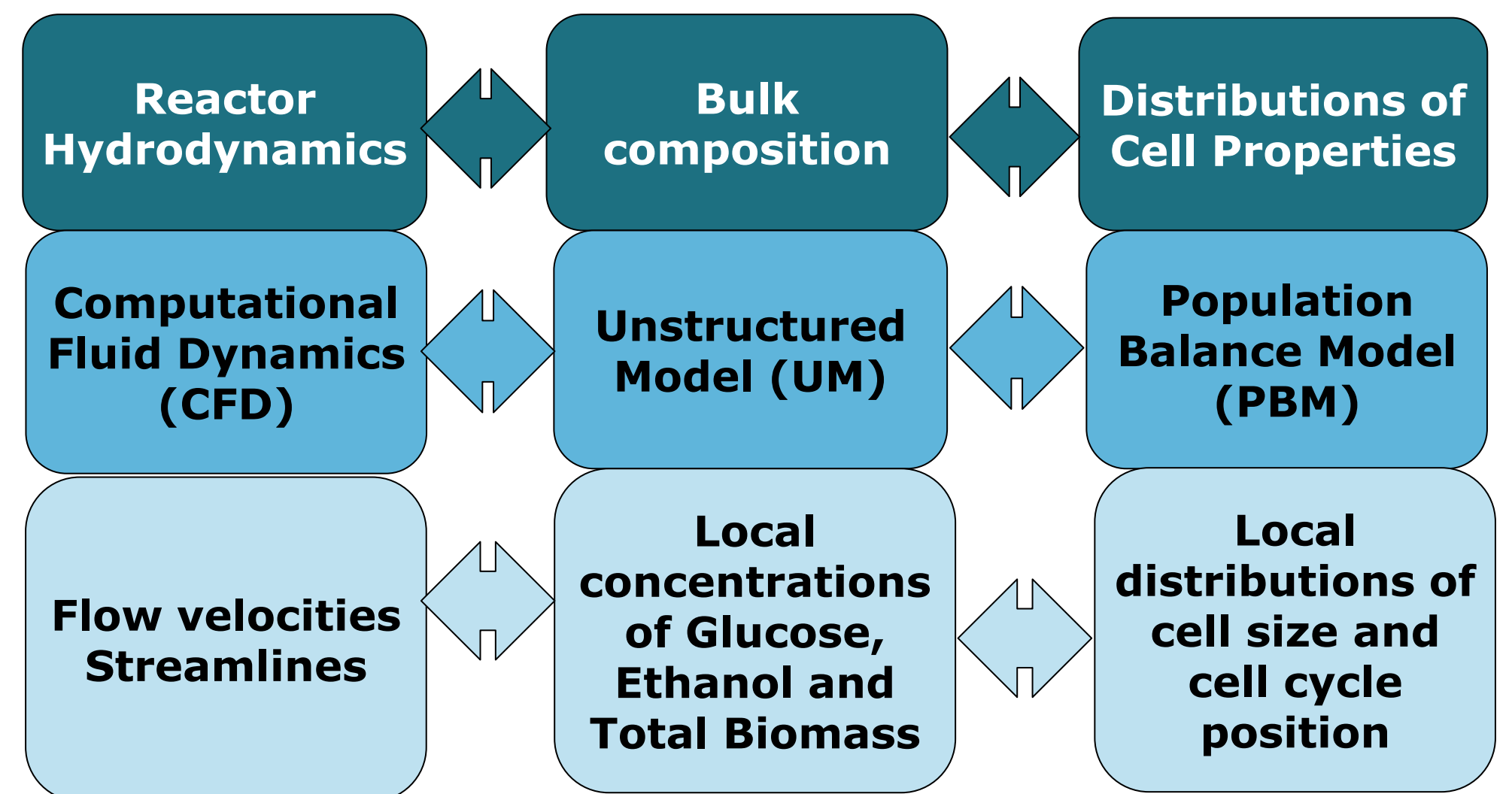
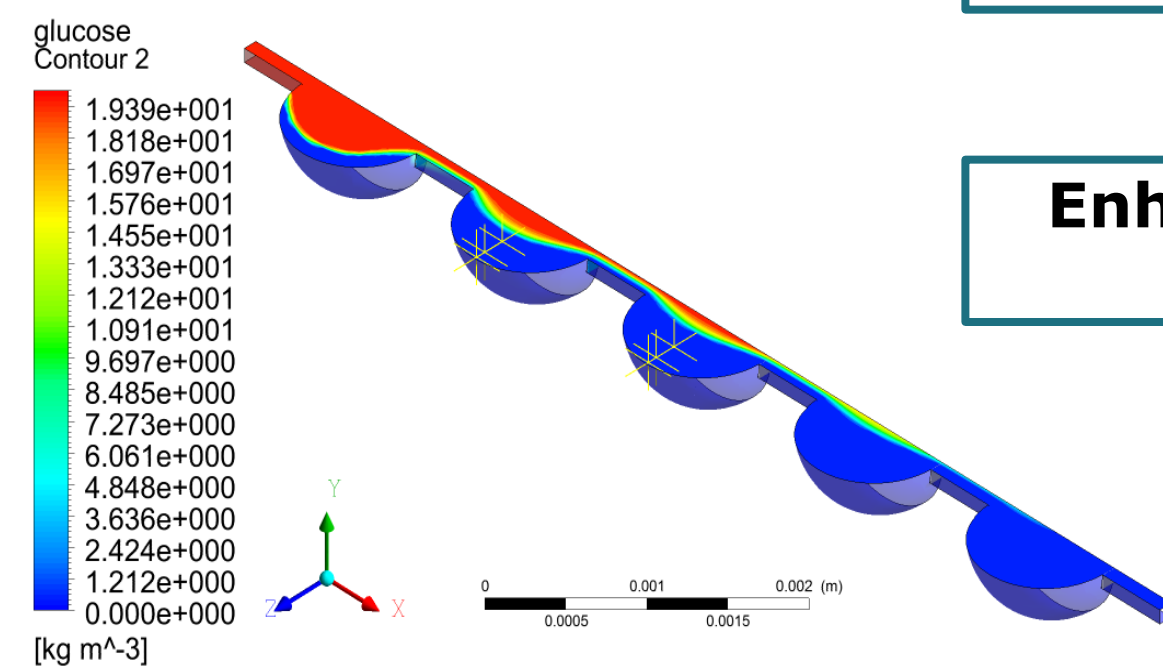
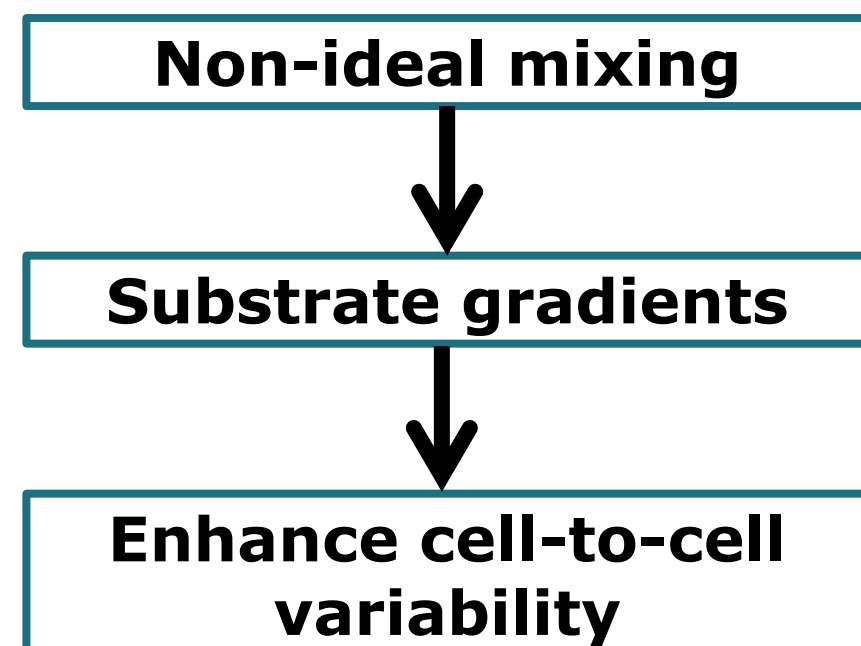
<sup>1</sup> PROCESS - Dept. of Chemical and Biochemical Engineering, Technical University of Denmark

<sup>2</sup> BIOMATH- Dept. of Mathematical Modelling, Statistics and Bioinformatics, Ghent University

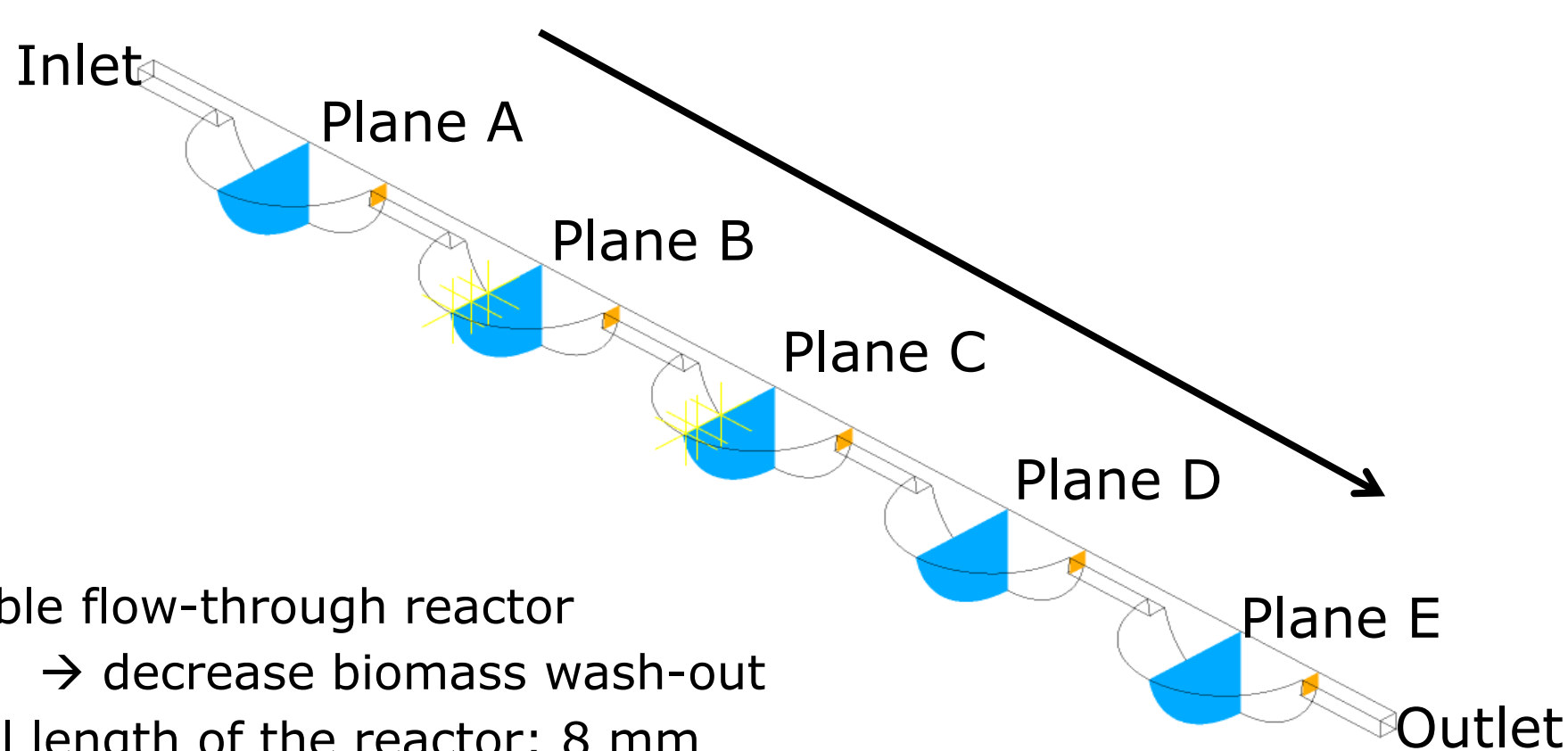
<sup>3</sup> CHEC - Dept. of Chemical and Biochemical Engineering, Technical University of Denmark



## Studying the development of cell property distributions in the presence of spatial substrate gradients

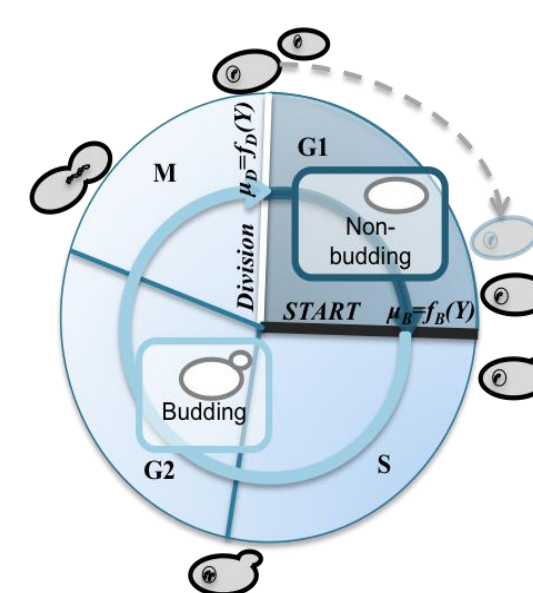


## Case study: Microbioreactor



- Bubble flow-through reactor  
→ decrease biomass wash-out
- Total length of the reactor: 8 mm
- Anaerobic growth of budding yeast
- Slow feed of glucose: 1 nL/s vs. 0.1 nL/s
- Laminar flow
- Incompressible fluids
- Diffusion is *not* taken into account
- Implemented in CFX 12.1 and the biological model was implemented using CEL language
- Hexaedral mesh with 32159 elements and 36535 nodes
- PBM discretized in 2x 20 pivots using the fixed-pivot method

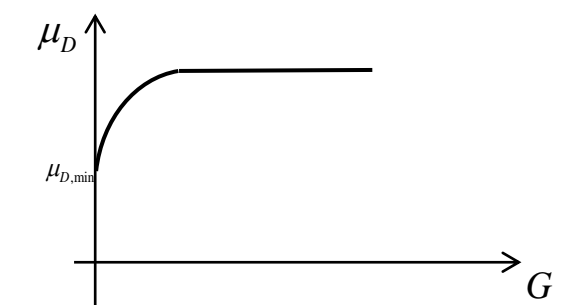
## 2-stage cell size structured PBM...



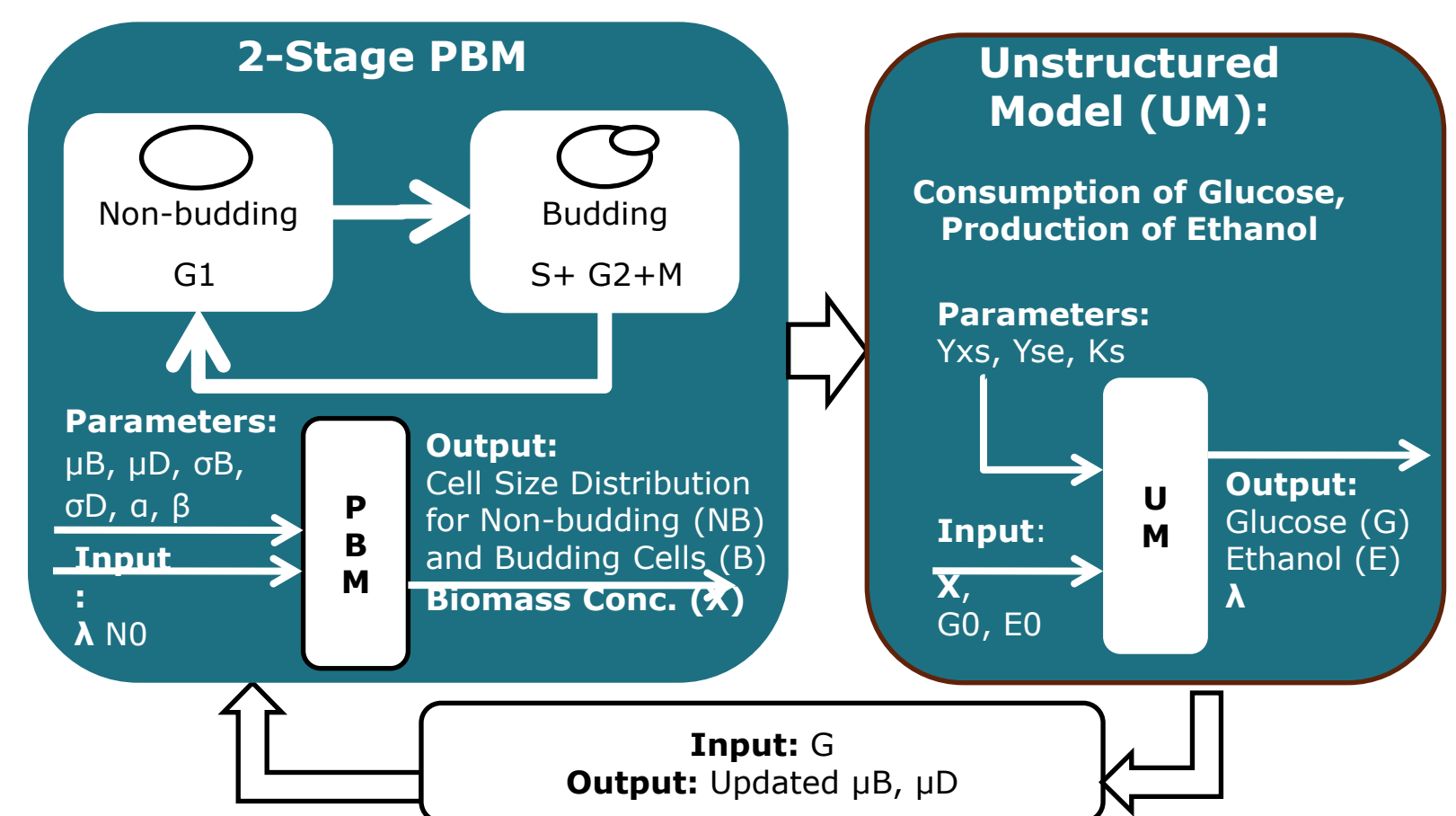
### Critical Budding and Division Sizes as functions of the substrate concentration

$$\mu_B = k_B \frac{G}{G + K_{BG}} + \mu_{B,min}$$

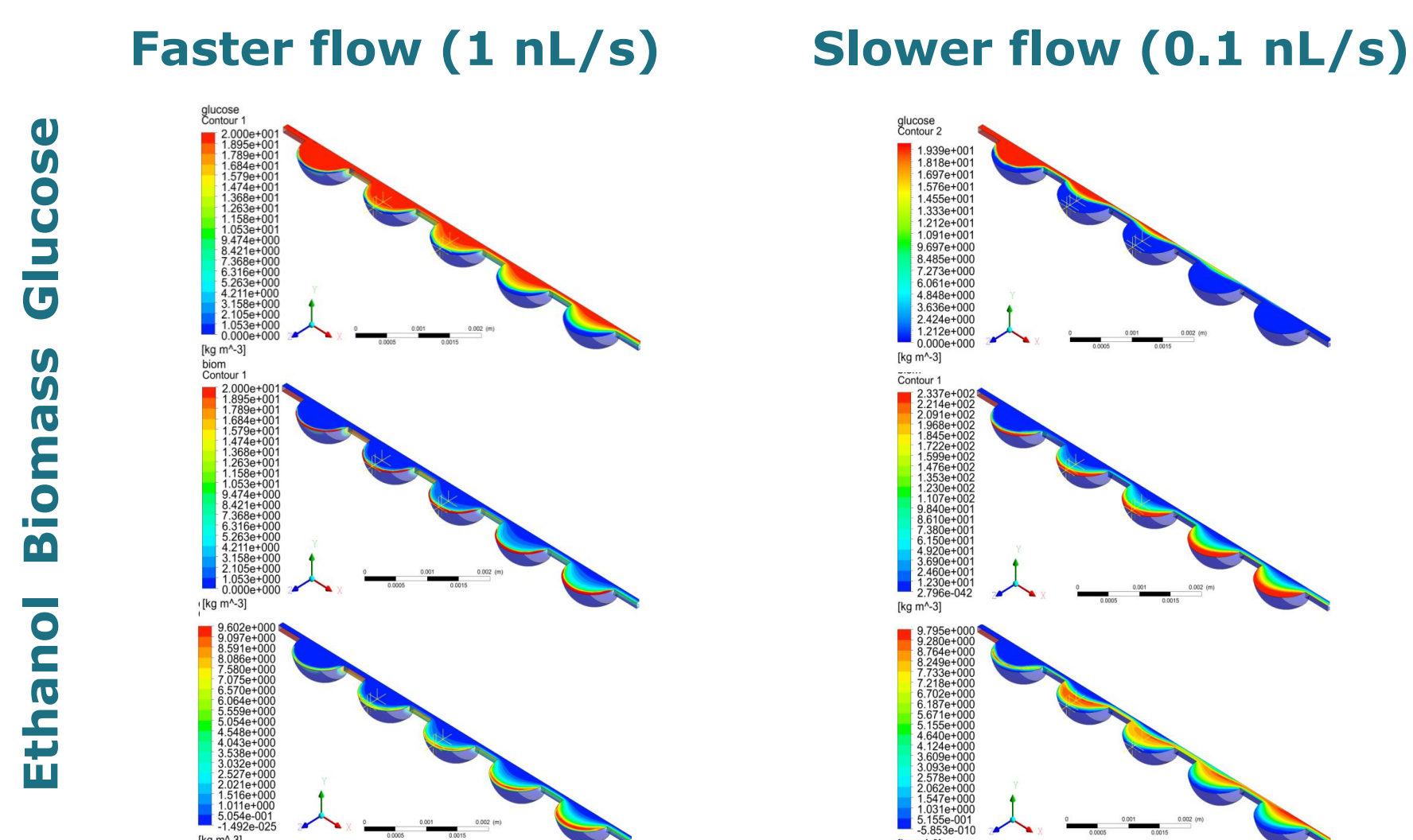
$$\mu_D = k_D \frac{G}{G + K_{DG}} + \mu_{D,min}$$



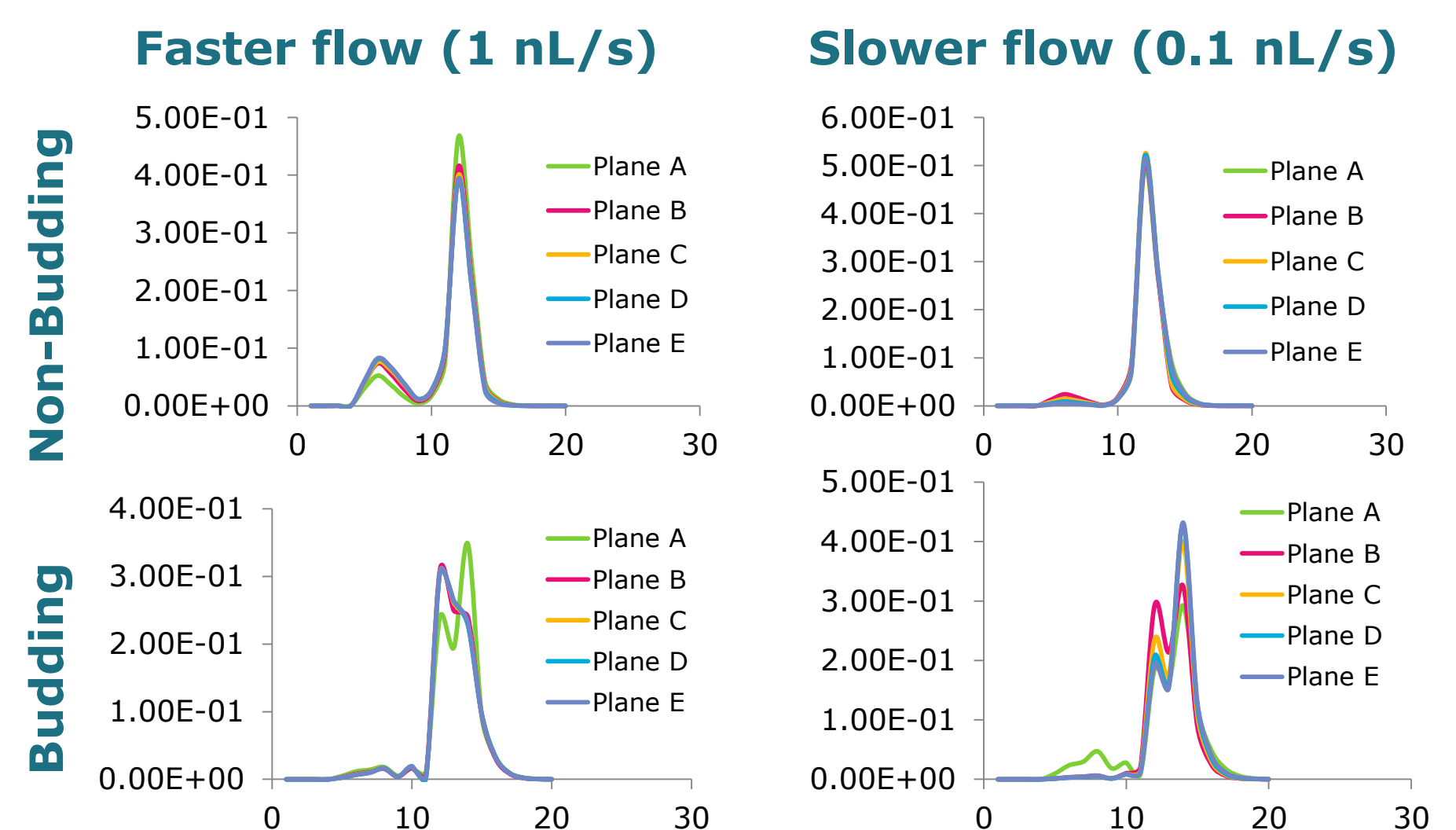
### ... coupled to an unstructured model



## Concentration profiles



## Local Concentrations and distributions



## Conclusion & Outlook

- Challenge in understanding the local distributions as they result from the interplay of flow and the population dynamics
- Proof-of-concept of integration of a CFD and PBM for multi-scale biological applications.
- In silico* simulation of various scenarios: different flow conditions, cellular kinetics, etc.
- Experimental Validation: overall distribution of biomass, bulk concentrations and cell distributions at the outlet



**Rita Lencastre Fernandes**  
Center for Process Engineering and Technology  
Dept. Chemical and Biochemical Engineering  
Technical University of Denmark  
rlf@kt.dtu.dk

### Acknowledgments

Danish Council for Strategic Research (Project no. 09-065160) and ERA-Net Industrial Biotechnology (Project no. EIB.08.031) are acknowledged for the financial support.

