University of Central Florida

COMSOL CONFERENCE 2014 BOSTON

Simulation of Gravity-Driven Flow Through a Microfluidic Device on a Rocker Platform

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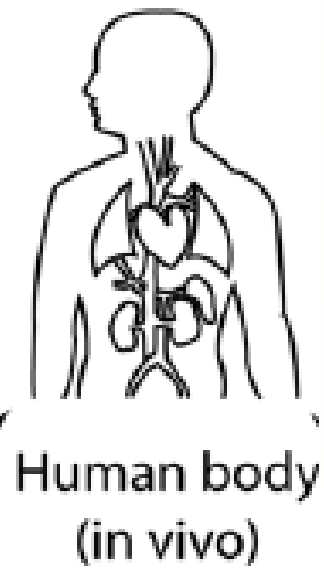
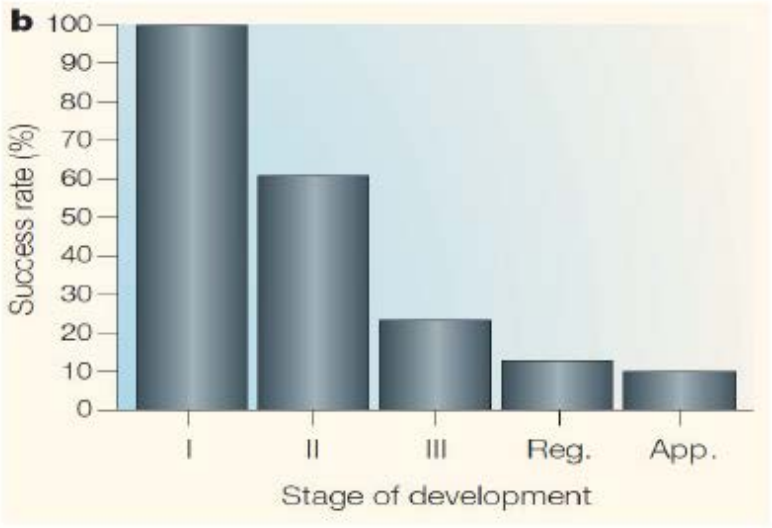
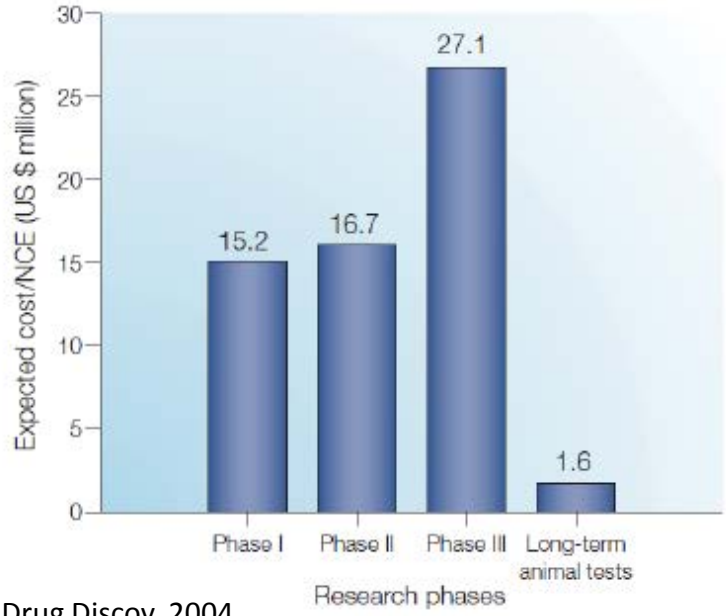
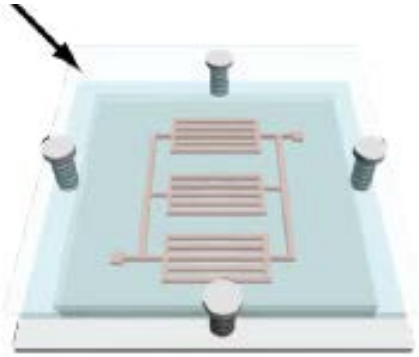
Drug development costs and microscale cell culture analog(μCCA)







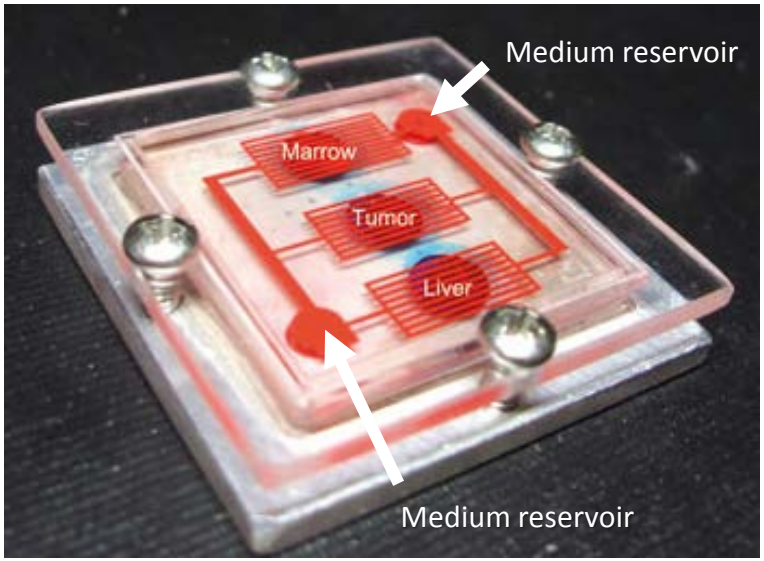
Kola & Landis, Nat Rev Drug Discov, 2004
Dickson,Nat Rev Drug Discov, 2004



Shuler Lab, Cornell University

- 1 in 10 drugs entering phase 1 gets approved
- Testing is expensive and time consuming
- Ethical issue: Animal testing

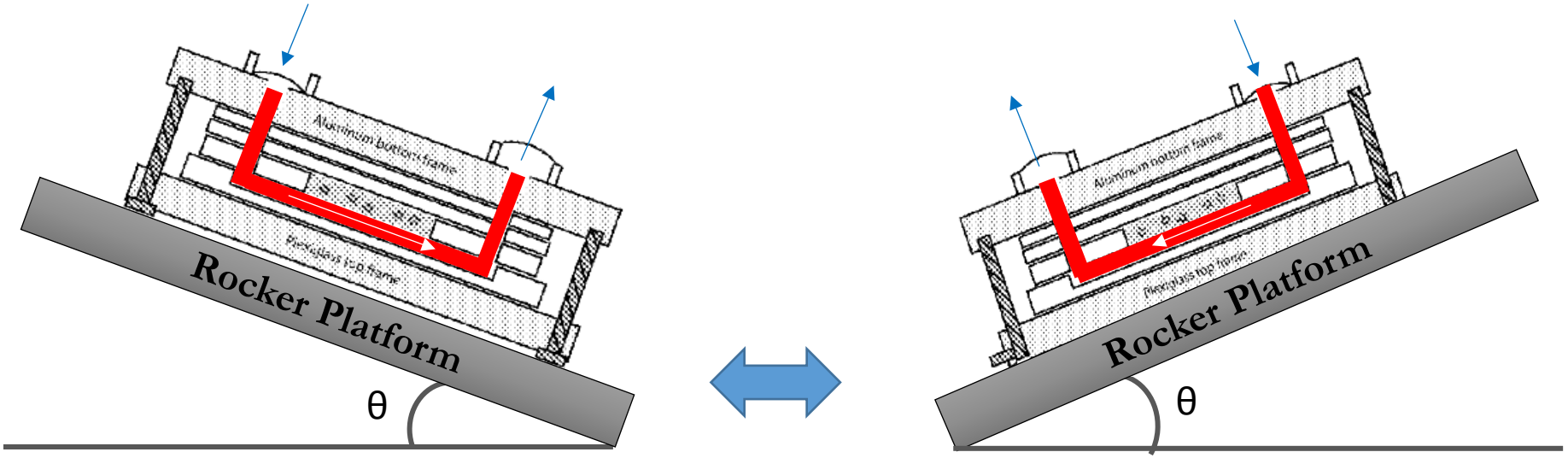
Simulations: Need?



µCCA for 3D cell culture, Shuler Lab, Cornell University

- Microfluidic device for organ-on-chip applications
- Drug testing
  - Drug diffusion and consumption
- Oxygen consumption
  - Hypoxia
- Cells are subjected to shear stress – mechanotransduction
  - Morphology, physiology
  - Physiological shear stress range – organ dependent
  - Shear stress estimation
  - Flow rates and velocity

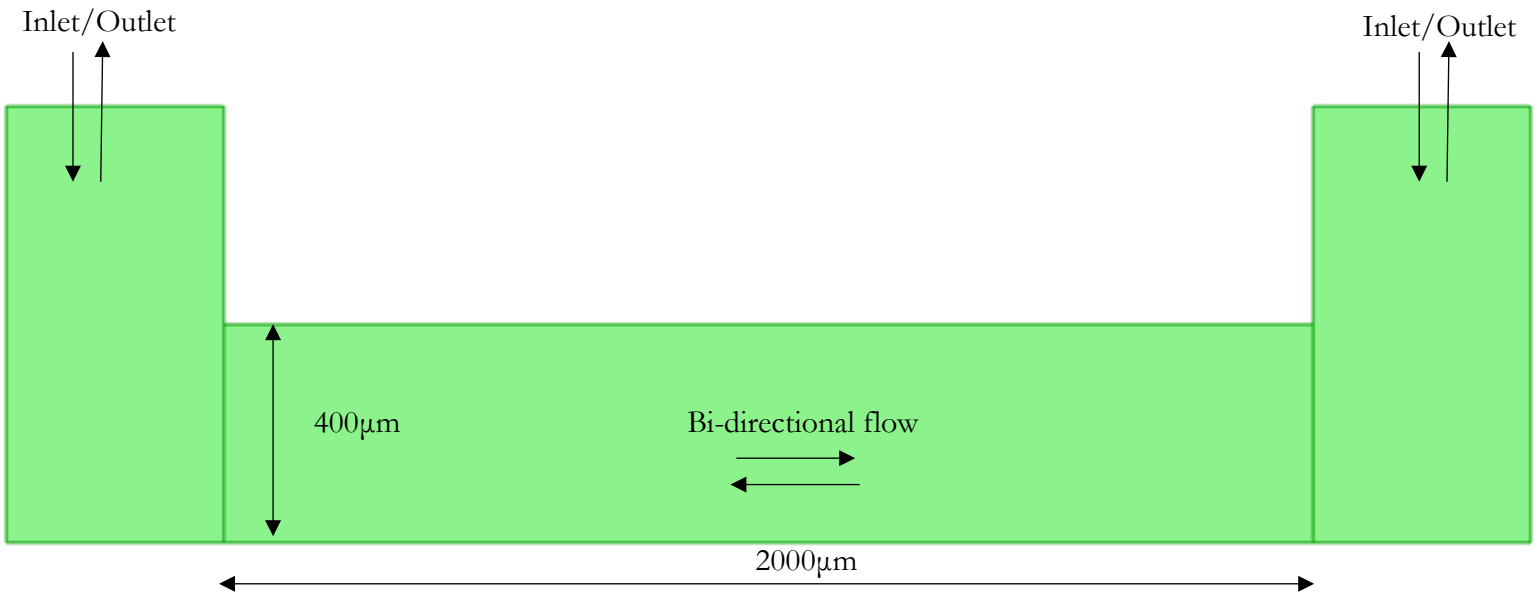
Gravity-driven flow through a microfluidic device

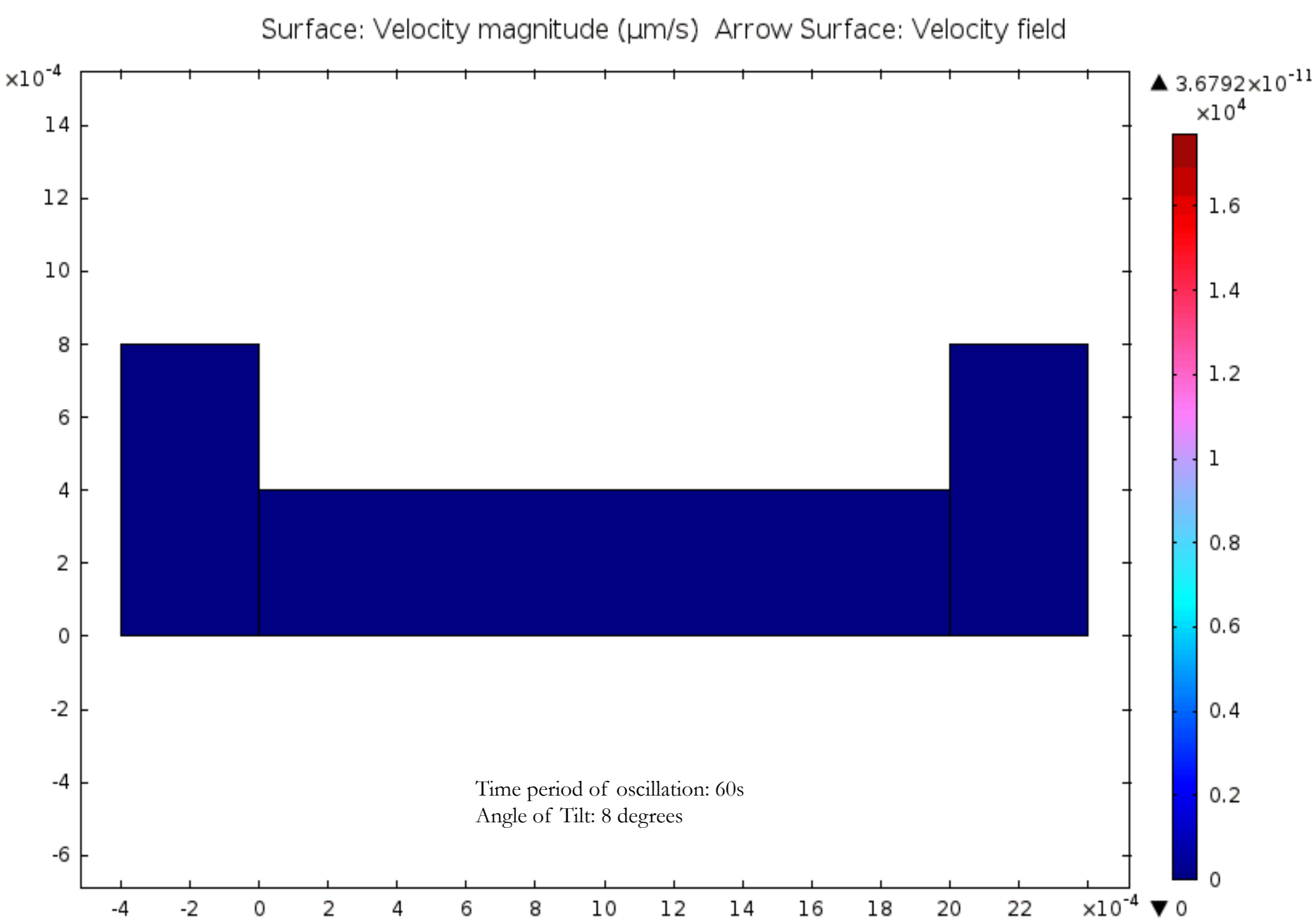


- Medium is recirculated by reciprocating tilting with rocker platform
- Gravity-induced flow naturally eliminates bubble problem
- No external pumps and tubing – reduces footprint of the device

Simulation of gravity driven bi-directional flow

- Module: Fluid flow → "Laminar Flow"
  - Incompressible flow, cell culture medium (viscosity, density)
- gravitational body force
  - Variable: frequency of oscillation
  - Angle of Tilt




Surface: Velocity magnitude (µm/s) Arrow Surface: Velocity field
×10^-4
14
12
10
8
6
4
2
0
-2
-4
-6
-4 -2 0 2 4 6 8 10 12 14 16 18 20 22 ×10^-4
▲ 3.6792×10^-11
×10^4
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
▼ 0
Time period of oscillation: 60s
Angle of Tilt: 8 degrees

Oxygen consumption within tissue

- Oxygen consumption rate in tissue: follows Michaelis-Menten type reaction
  - $R = K_{max} * C/(C + M)$
  - $K_{max} = 0.034$ mol/m^3/s (max. O2 consumption rate)
  - M = Michaelis-Menten constant; $=1.0\times10^{-3}$ mol/m^3

Vary with tissue type

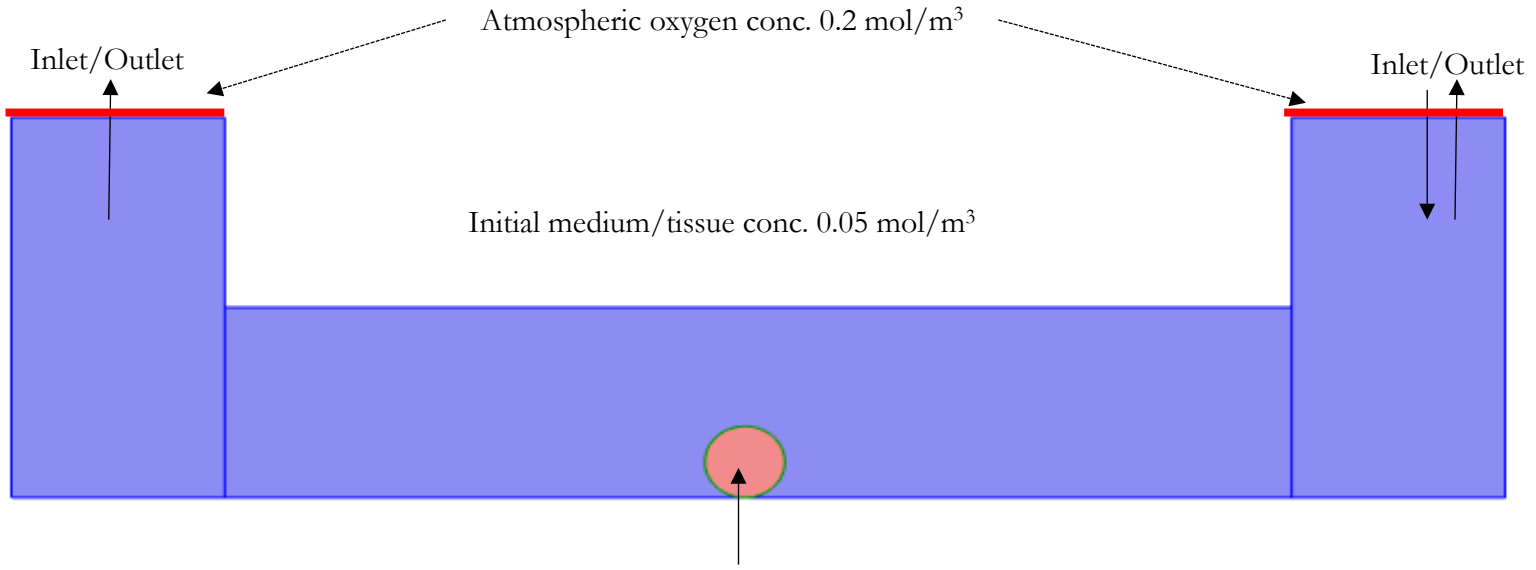
- Oxygen concentrations and diffusion:
  - $C_{atm} = 0.200$ mol/m^3
  - C_{tissue} initial $= 0.05$ mol/m^3
  - Diffusion Constants:
    - $D_w = 3.0\times10^{-9}$ m^2/s (O_2 in water);
    - $D_t = 2.0\times10^{-9}$ m^2/s (O_2 in tissue)

Simulation of gravity driven bi-directional flow with oxygen diffusion and consumption in a tissue

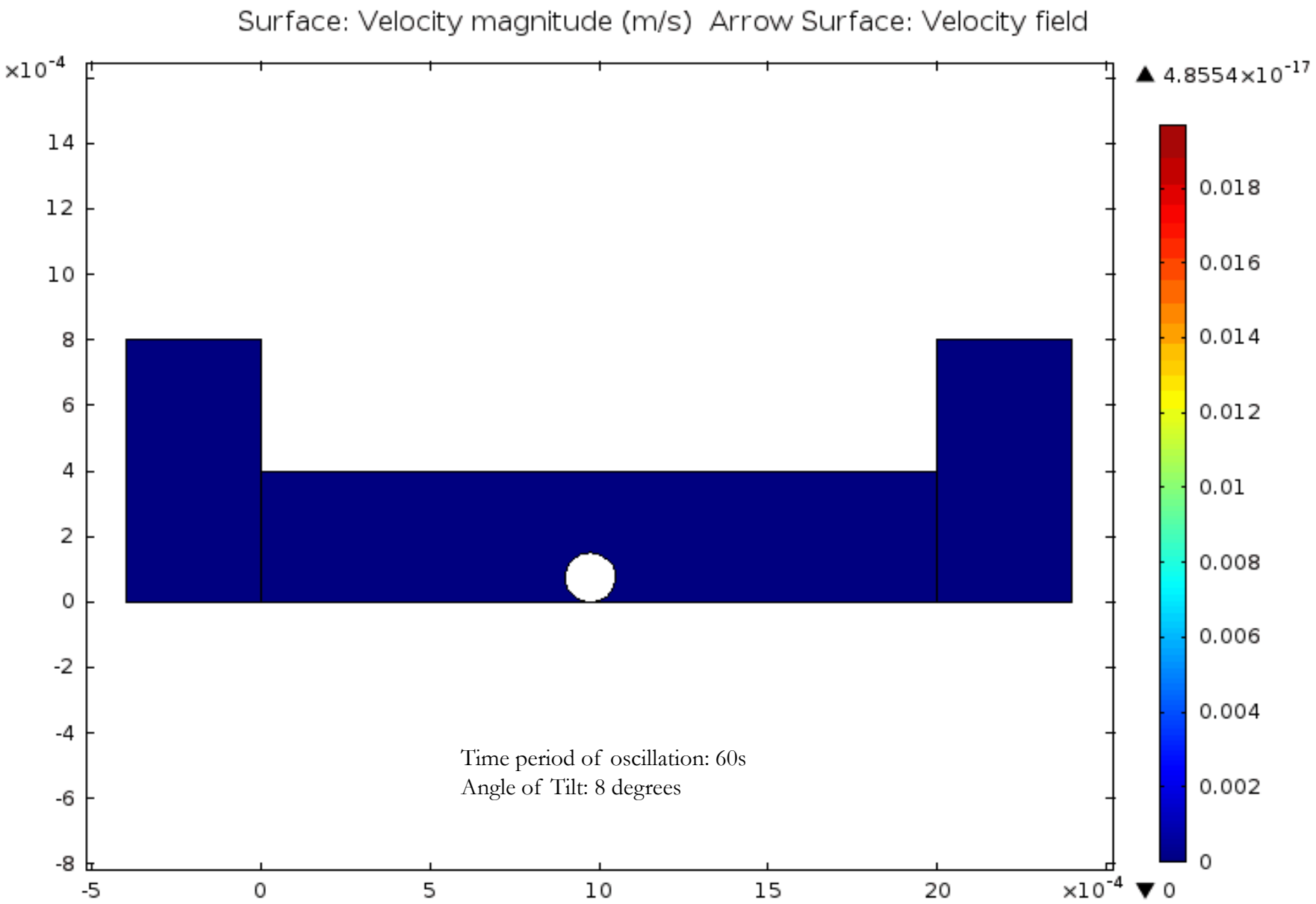
- Module:

Chemical Reaction Engineering → "Transport of dilute species" + Fluid flow → "Laminar Flow"

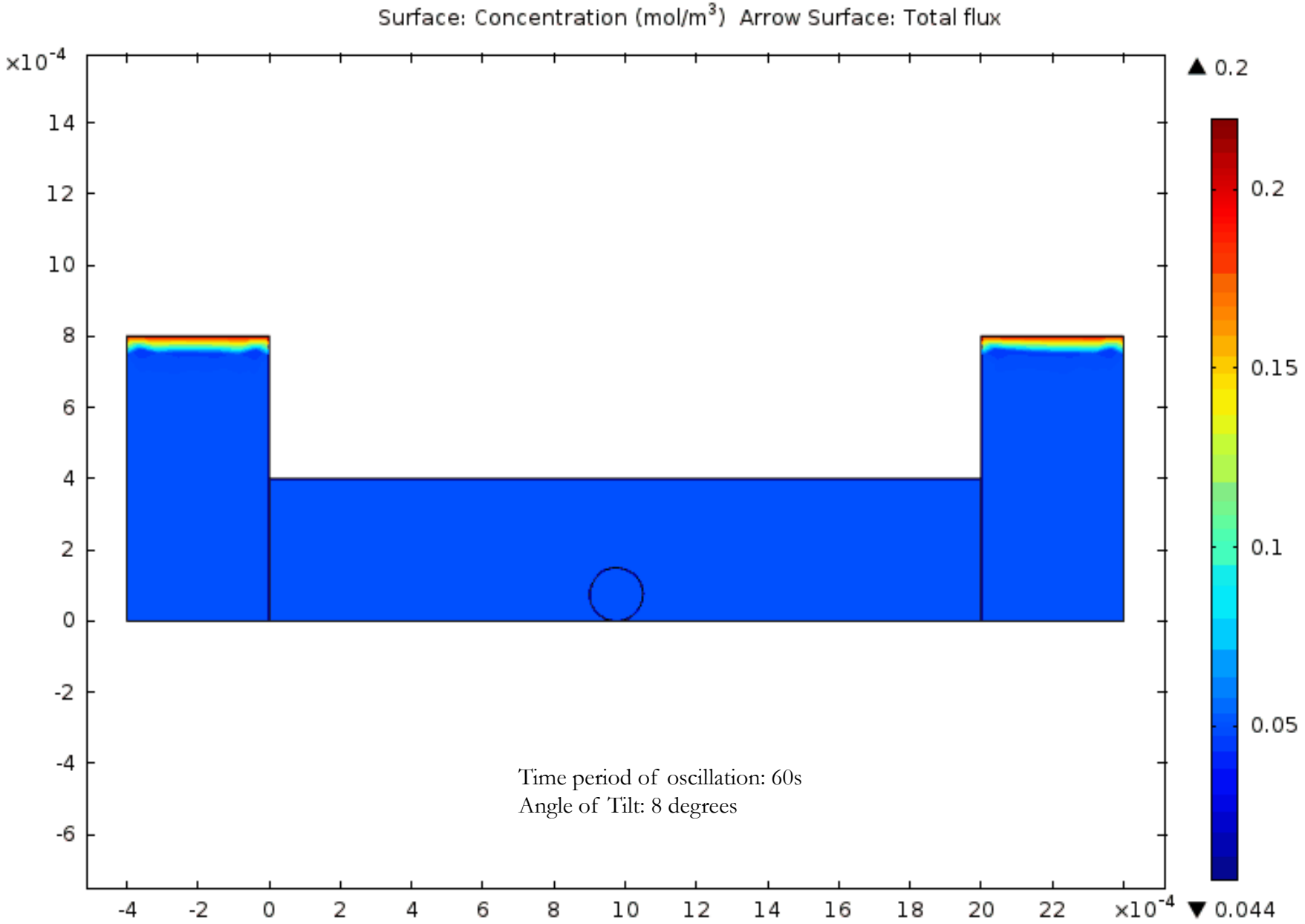
- Solve flow first and then use flow results as input for transport of dilute species



Bi-directional flow around the tissue



Bi-directional flow around the tissue
Oxygen diffusion and consumption



Drug diffusion and consumption within tissue Simulation Approach

- Drug consumption rate in tissue: follows Michaelis-Menten type reaction
  - $R = K_{max} * C/(C + M)$
  - K_{max} (max. drug consumption rate)
  - M = Michaelis-Menten constant

Vary with tissue/enzyme/drug combination

- Oxygen concentrations and diffusion:
  - C_{drug} and C_{tissue}
  - Diffusion Constants:
    - D_w (drug in culture medium);
    - D_t (drug in tissue)

Conclusions

- Simulation models
  - Bi-directional gravity driven flow
  - Diffusion
  - Consumption of oxygen/ drugs in tissue based on Michaelis-Menten type Reactions

- Design of microfluidic systems
  - Physiological shear stress
  - Drug diffusion times
  - Drug concentration/distribution within the device
  - Drug consumption rates