Early development drug formulation on a chip: Fabrication of nanoparticles using a microfluidic spray dryer

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Supplemental Information

This supplemental information contains details of the simulation model that has been developed to study the deformation of the channel geometry of our microfluidic spray dryer and its impact on the flow profile inside the device. If you have additional questions, feel free to send an email to julian.thiele@uni-bayreuth.de.

Analysis of the flow pattern of a flow-focused aqueous solution of Rhodamine B in a microfluidic device shows that the surface contact between the dye solution and the channel walls decreases with increasing channel height, as shown in Figure S1.

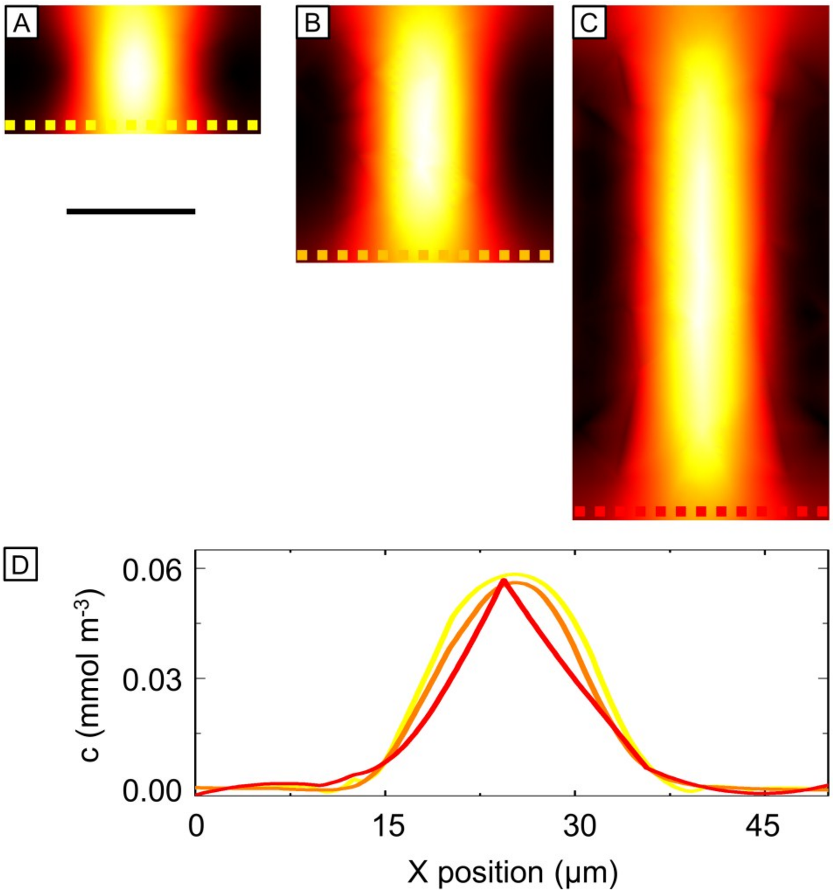

Fig. S1 Finite element simulation of a flow-focused fluid stream of Rhodamine B in water in microchannels with a constant width of 50 µm and varying heights of (A) 25 µm, (B) 50 µm and (C) 100 µm. The plane-cuts, which show the concentration profile of Rhodamine B, and (D) the corresponding line scans reveal that the surface contact between the dye solution and the microchannel walls decreases from low to high aspect ratios. The scale bar denotes 25 µm.

We analogously develop a device with a high aspect ratio to minimize the surface contact of the danazol-loaded solvent stream with the channel walls. Thus, fouling of the device due to adsorption of the hydrophobic drug on the microchannel walls can be prevented. However, PDMS microchannels with a high-aspect ratio are less pressure-resistant than squared channels and expand at high flow rates and high air pressure. To study the impact of the channel deformation on the flow profile, we use COMSOL Multiphysics v4.1.0.185, which allows simulating coupled multiphysics problems, such as the solid mechanics of PDMS that are coupled with the fluid dynamics in the case at hand. The tasks for developing the simulation model are illustrated in Figure S2.

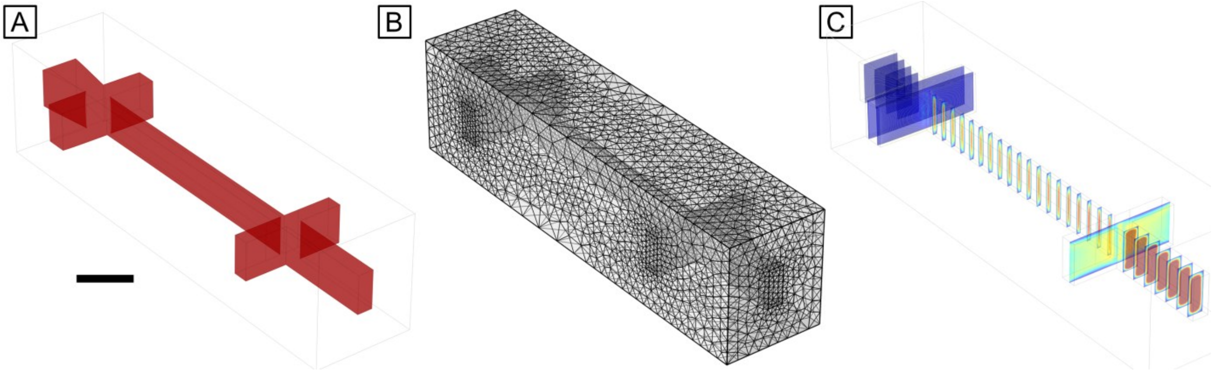

Fig. S2 Towards the simulation of the fluid flow inside the microfluidic spray dryer at low flow rates and low air pressure: (A) Import of the 3D device geometry drawn in AutoCAD 2011, (B) mesh generation and (C) solution of the model. The scale bar denotes 100 µm.

In a first step, a model of the device section of interest, which we design using AutoCAD 2011, is imported to COMSOL. Thereafter, the boundary conditions are assigned to the microchannel walls, the inlets and the outlet of the device assuming stationary conditions. Thereby, the fluid dynamics are described by the Navier-Stokes equations which can be simplified assuming incompressible fluids, thus ρ = const.[1]

$$\rho\nabla\cdot\mathbf{u}=0$$

$$\rho\frac{\partial\mathbf{u}}{\partial t}+\rho(\mathbf{u}\cdot\nabla)\mathbf{u}=\nabla\cdot[-p\mathbf{I}+\mu(\nabla\mathbf{u}+\nabla\mathbf{u}^{\mathrm{T}})]+\mathbf{F}$$

with the density of the fluid ρ, the pressure p, the identity matrix **I**, the dynamic viscosity of the fluid μ, the velocity field **u** and the volume force **F**. The deformation of PDMS is simulated using COMSOL's linear elastic model which involves the following equations:[1]

$$-\nabla\cdot\sigma=\mathbf{F}_{\mathrm{v}}$$

$$\sigma=\big(\mathbf{S}\cdot(\mathbf{I}+\nabla\mathbf{u})\big)$$

$$\mathbf{S}-\mathbf{s}_0=\mathbf{C}:(\varepsilon-\alpha(\mathrm{T}-\mathrm{T}_{\mathrm{Ref}})-\varepsilon_0)$$

$$\varepsilon=\frac{1}{2}(\nabla\mathbf{u}^{T}+\nabla\mathbf{u}+\nabla\mathbf{u}^{T}\nabla\mathbf{u})$$

with the stress tensor $\mathbf{S}$, the strain tensor ε, the 4th order elasticity tensor $\mathbf{C}$, the initial stresses $\mathbf{s}_0$, the initial strains ε_0, the thermal expansion tensor α and the (reference) temperature T (T_{Ref}). The specific material properties are then defined, as listed in Table S1.

Tab. S1 Material properties used in the simulation model.

Name	**Value**
Young's modulus (E_{PDMS})[2]	4 MPa
Poisson's ratio (ν_{PDMS})[2]	0.42
Density of PDMS (ρ_{PDMS})[3]	920 kg m^{-3}
Density of water (ρ_{Water})[4]	998.2 kg m^{-3}
Dynamic viscosity (η_{Water})[4]	$1.002 \cdot 10^{-3}$ kg m^{-1} s^{-1}
Main channel inlet ($v_{MC,slow}$)	0.02867 m s^{-1}
Side channel inlet ($v_{SC,slow}$)	0.2525 m s^{-1}
Pressure (p_{slow})	0.34 bar
Main channel inlet ($v_{MC,fast}$)	0.1434 m s^{-1}
Side channel inlet ($v_{SC,fast}$)	1.263 m s^{-1}
Pressure (p_{fast})	2.09 bar

The model is solved for 62713 finite elements and 401878 degrees of freedom using a multifrontal massively parallel solver (MUMPS). The average element quality of the mesh is 0.8003 on a scale from 0 to 1, where 1 is the highest quality; the minimal element quality is 0.3903. Using a Windows 7 x64 machine with two quad-core Intel® Xeon® E5440-processors operating at 2.83 GHz and an internal memory of 32 GB RAM, the less complex model of the microfluidic spray dryer at low flow rates and low pressure is solved in 1307 s, and the model of the microfluidic device operating at high flow rates and high air pressure is solved in 2700 s.

References

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