

## Supporting Information S3

### A Numerical Investigation of Intrathecal Isobaric Drug Dispersion within the Cervical Subarachnoid Space

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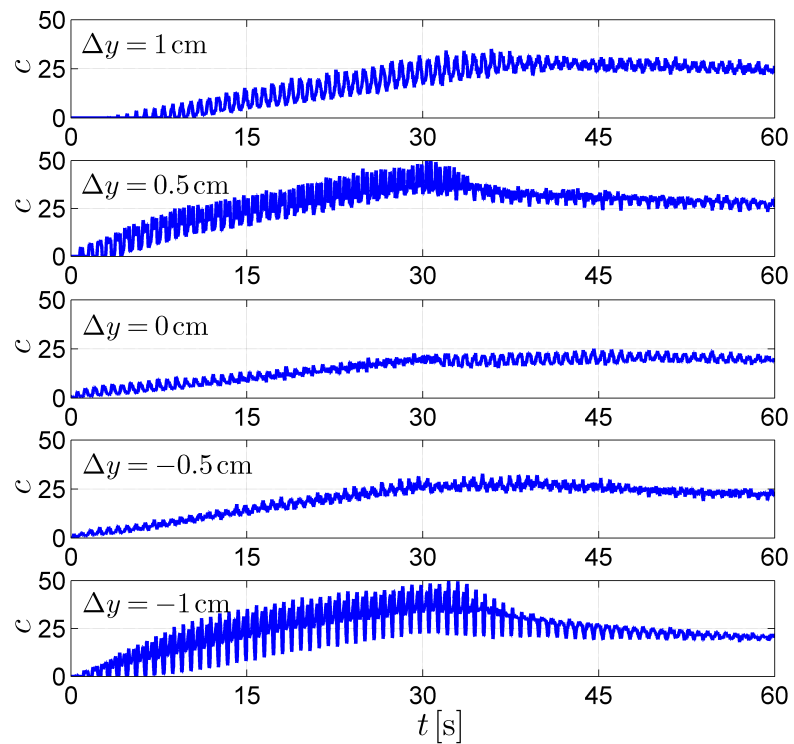
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### Concentration trend after injection

In the present study we considered a limited time window (20 cardiac cycles, i.e. nearly 15 s) because of the computational costs inherently associated with the adopted forward-modeling approach with physics resolved both in space and time. To qualitatively assess the effect of the injection termination, we also ran a longer simulation. In particular, we considered a 60 s time window during which we only injected over the initial 30 s. With regard to the injection parameters, we adopted those of test case S<sub>1</sub> (injection at P<sub>1</sub>,  $\theta=0^\circ$ ,  $\phi=0^\circ$ ,  $\bar{v}_{inj}=6$  cm/s).

Exemplary numerical results for the evolution of drug concentration are reported in Fig.1, where  $c$  represents a normalized drug concentration on a fixed cross-section at a distance of  $\Delta y$  from the injection point. In particular, we divided the concentration in a thin volume slice (0.8 mm thick) centered at the considered cross-section by the total average concentration in the whole domain after 10 cycles. It should be noted that  $c$  linearly increased during injection, while it tends to flatten and decrease when the injection stopped. Qualitatively speaking, these results describe the expected gradual decrease in drug concentration after injection, consistent with prior numerical results [1, 2].



**Fig 1. Particle concentration after injection.** Temporal profile of the normalized drug concentration obtained with perpendicular injection at  $P_1$  for selected distances  $\Delta y$  from the injection point and by stopping the injection after 30 s.

## References

1. Hsu Y, Hettiarachchi HDM, Zhu DC, Linninger AA. The frequency and magnitude of cerebrospinal fluid pulsations influence intrathecal drug distribution: key factors for interpatient variability. *Anesth Analg.* 2012 Aug;115(2):386–394.
2. Tangen KM, Hsu Y, Zhu DC, Linninger AA. CNS wide simulation of flow resistance and drug transport due to spinal microanatomy, *J Biomech.* 2015 Jul;48(10):2144–2154.