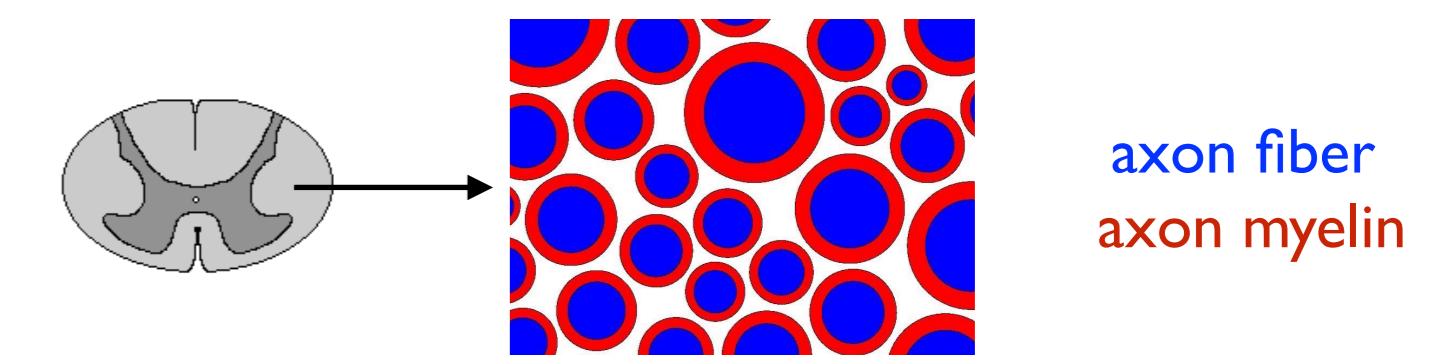


Introduction

Quantitative MRI provides micro-structural parameters such as the Myelin Volume Fraction (MVF) or the fraction restricted (fr) in white matter. However, acceptable values for these parameters, as well as their sensitivity to micro-structural variation (e.g. changes in axon density, axon diameter distribution, g-ratio) are not clear.

In this perspective, we provide a new random disks packing algorithm for numerical simulation of the white matter. While other algorithms exist, none of them allow the user to fix independently each micro-structural parameter, nor are they freely available.

From this tool, we derived multiple values of axon density and thus an acceptable range for fr and MVF.



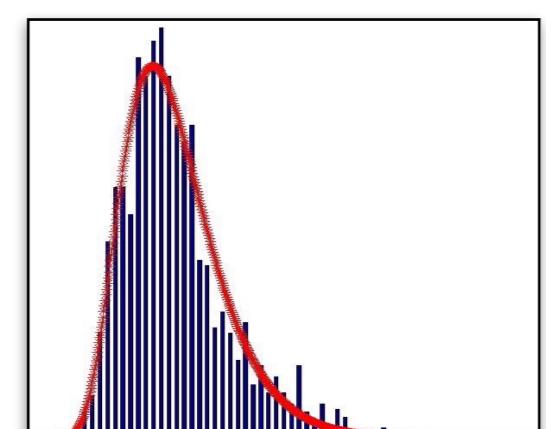
Methods

White matter model

White matter tissue was modelled as in [1], typically adapted for corpus callosum and spinal cord, with N parallel cylinders spaced from each other by a gap d of various radii following a lognormal distribution defined by σ and μ [2]. Due to the geometric consistency along the axonal fibers, the problem was reduced to a 2-dimensional packing of perfectly round and non-compressible disks. The simulator was implemented in Matlab [3]. Based on the input (σ , μ , d, N) it maximizes the disks' density ϕ .

Algorithm

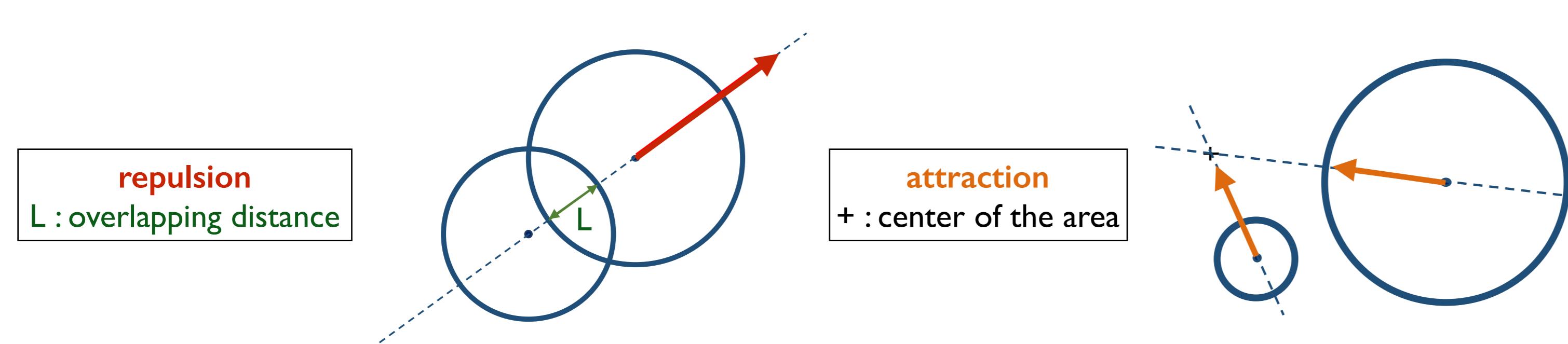
1. We first perform a sampling of disks' radii using Hastings-Metropolis algorithm.



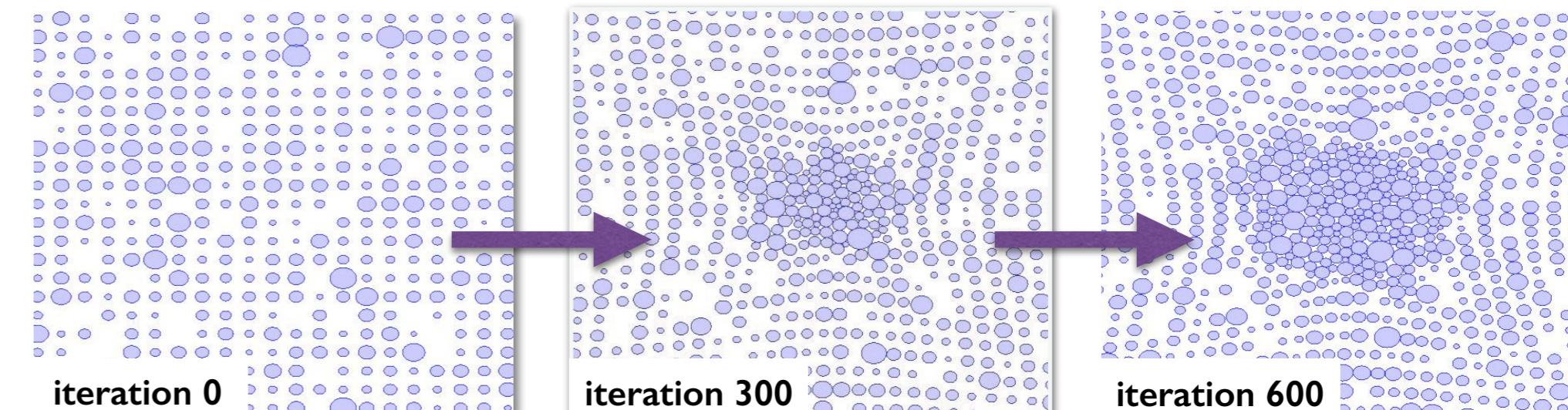
log-normal probability density function
histogram of radii after sampling

2. Then we randomly initialize disk positions in a square area and perform migrations of these disks with two constraints : attraction towards the center of the area and repulsion if disks overlap.

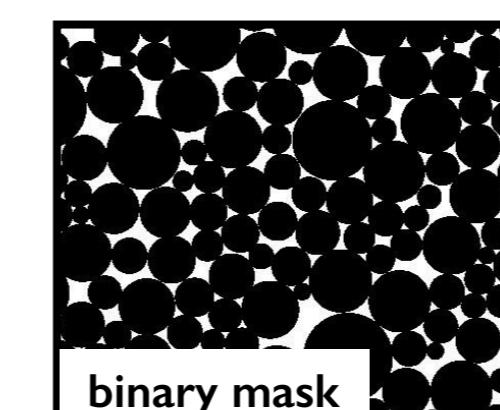
- **repulsion** direction is fixed by the disks' centres that overlap and its norm depends on the overlapping distance L.
- **attraction** to the center is the same for every disks but disappear if overlapping occurs.



Iteration process :



3. The software outputs binary masks that can easily provide MVF or fr from ϕ , assuming a constant g-ratio between 0.7 and 0.8.



$$\phi = \frac{\text{length}(\text{find}(\text{mask} == 1))}{\text{mask area}} \Rightarrow \begin{cases} fr = g^2 * \frac{\phi}{1+(g^2-1)*\phi} \\ MVF = (1-g^2) * \phi \end{cases}$$

Validation and exploitation of the software

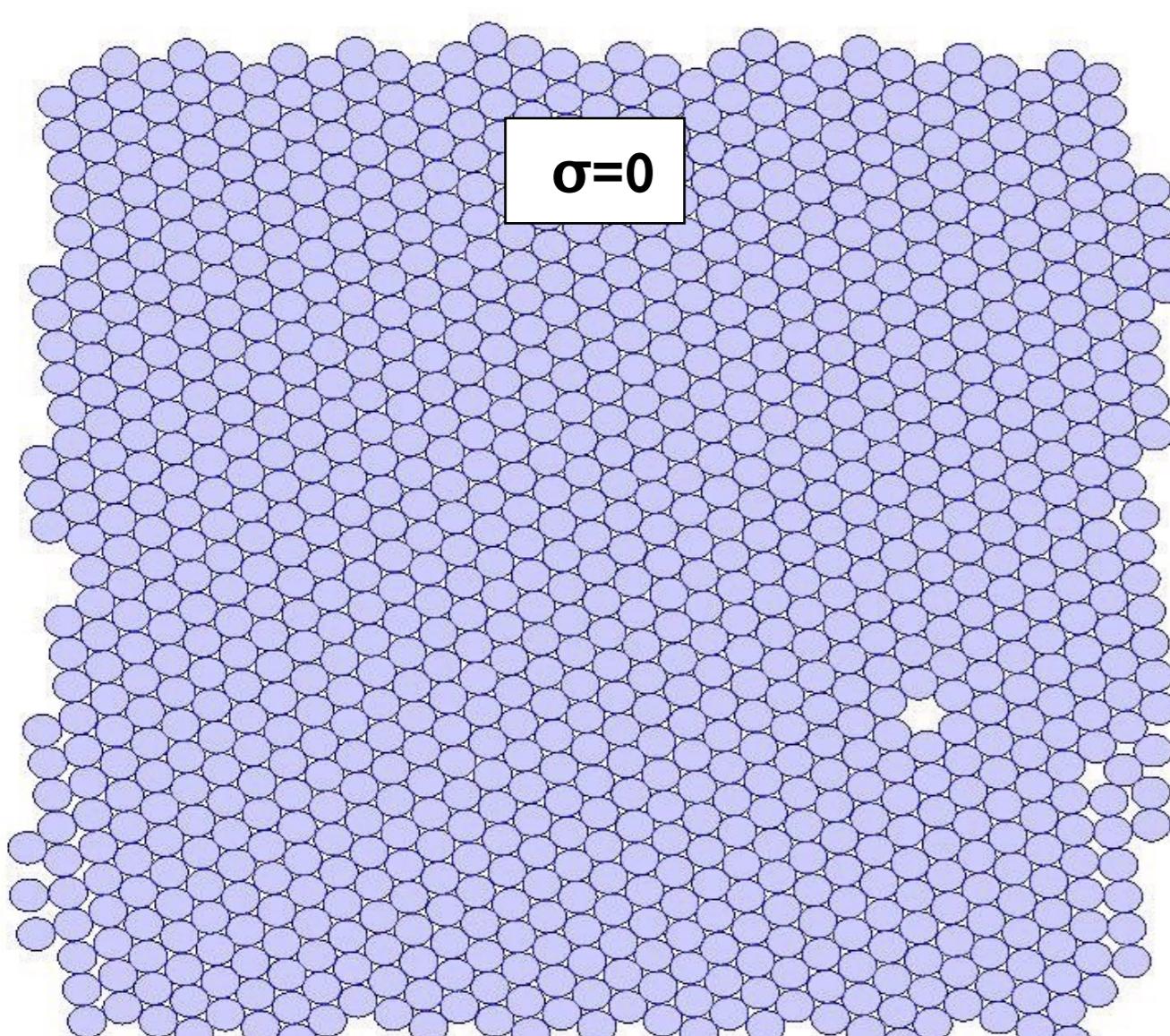
To validate the simulator we looked at the reproducibility over 50 runs for different case scenario.

- ① one single radius ($\mu = 3 \mu\text{m}$, $\sigma = 0$), no gap between axons ($d=0$). We expected to obtain the hexagonal closest packed structure where the theoretical density is $\pi/\sqrt{12}$ [4].
- ② lognormal radii distributions : $\mu = 3 \mu\text{m}$, $\sigma = [0.5 \ 1.5 \ 2.5] \mu\text{m}$, $d=0$. We wanted to estimate the variance of ϕ over the 50 runs.
- ③ varying d from 0.1 to 2 μm ($\mu=3\mu\text{m}$, $\sigma=1\mu\text{m}$, $g=0.72$ for each packing). This last scenario was used to get realistic ranges of fr and MVF.

N = 1000 axons and 1500 iterations were used for each simulation.

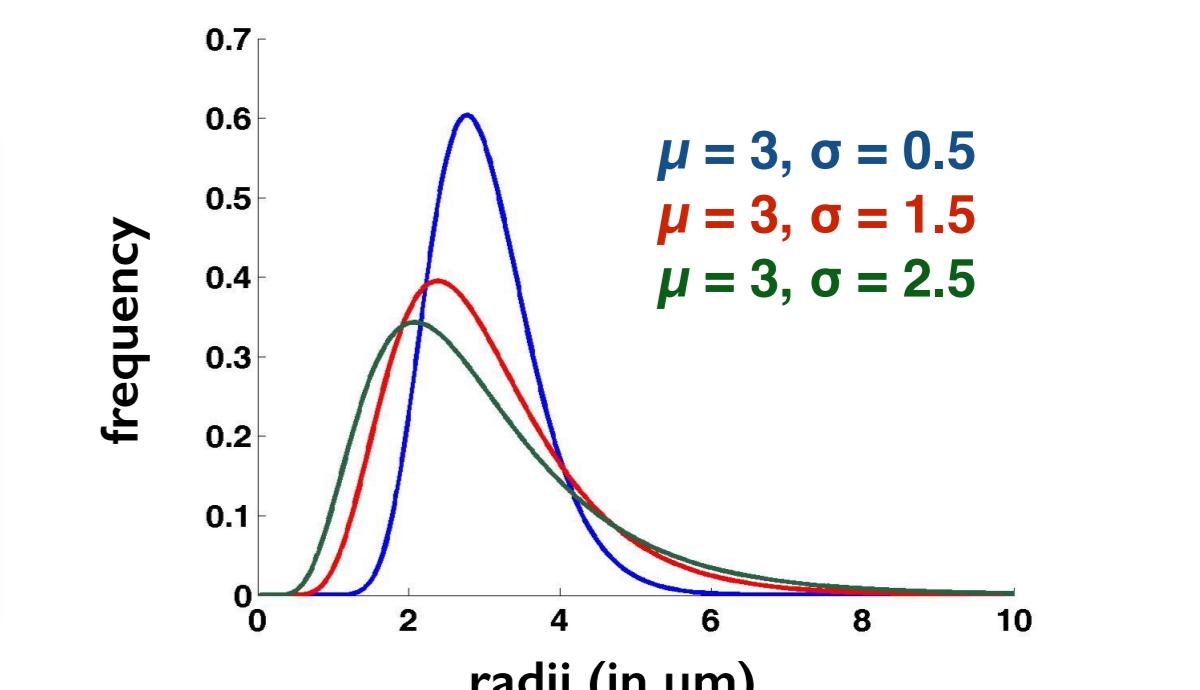
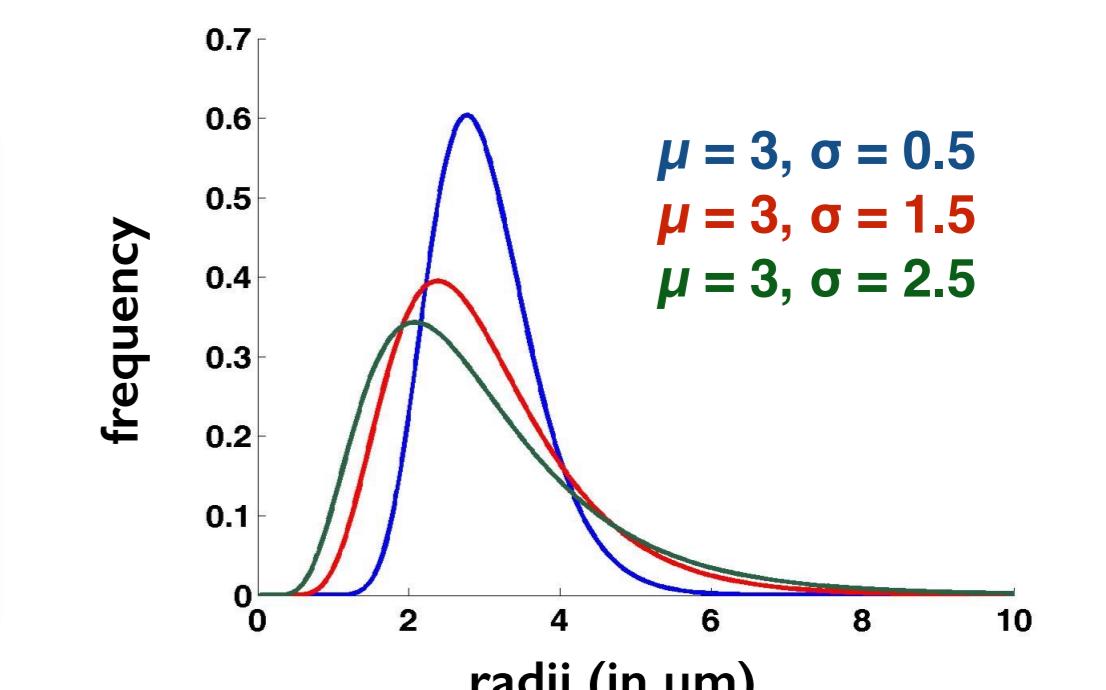
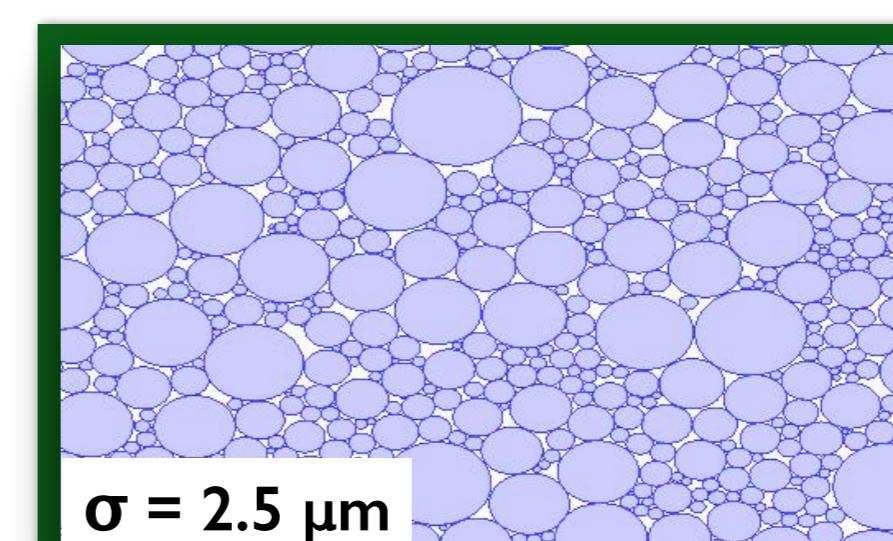
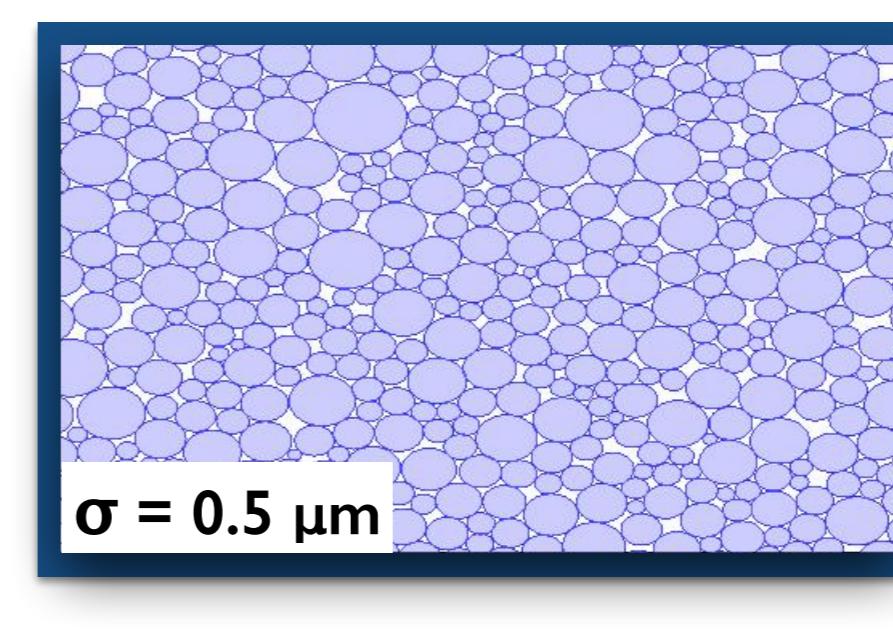
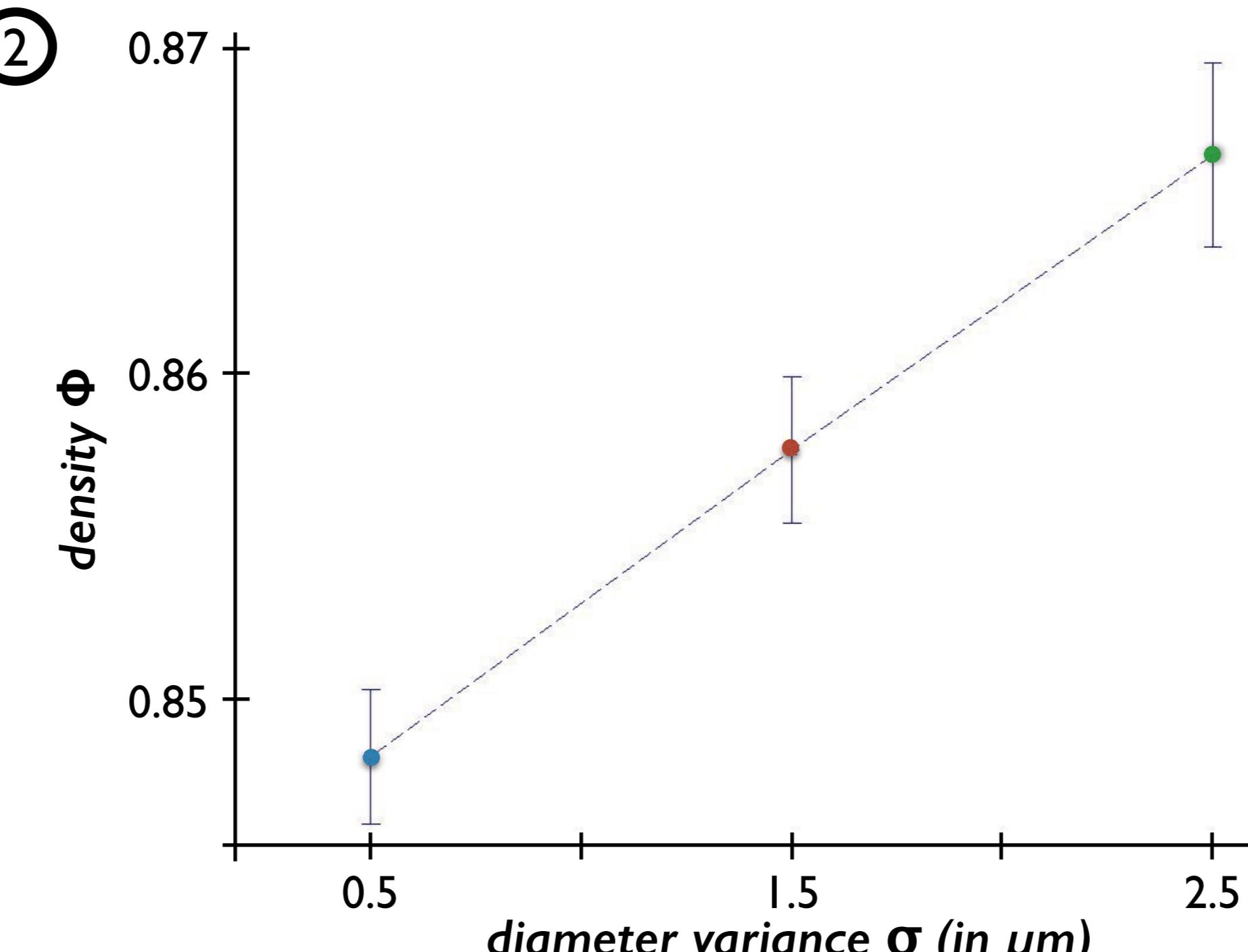
Results

1



$\Phi = 0.89$ is very closed to the theoretical density $\pi/\sqrt{12} = 0.91$

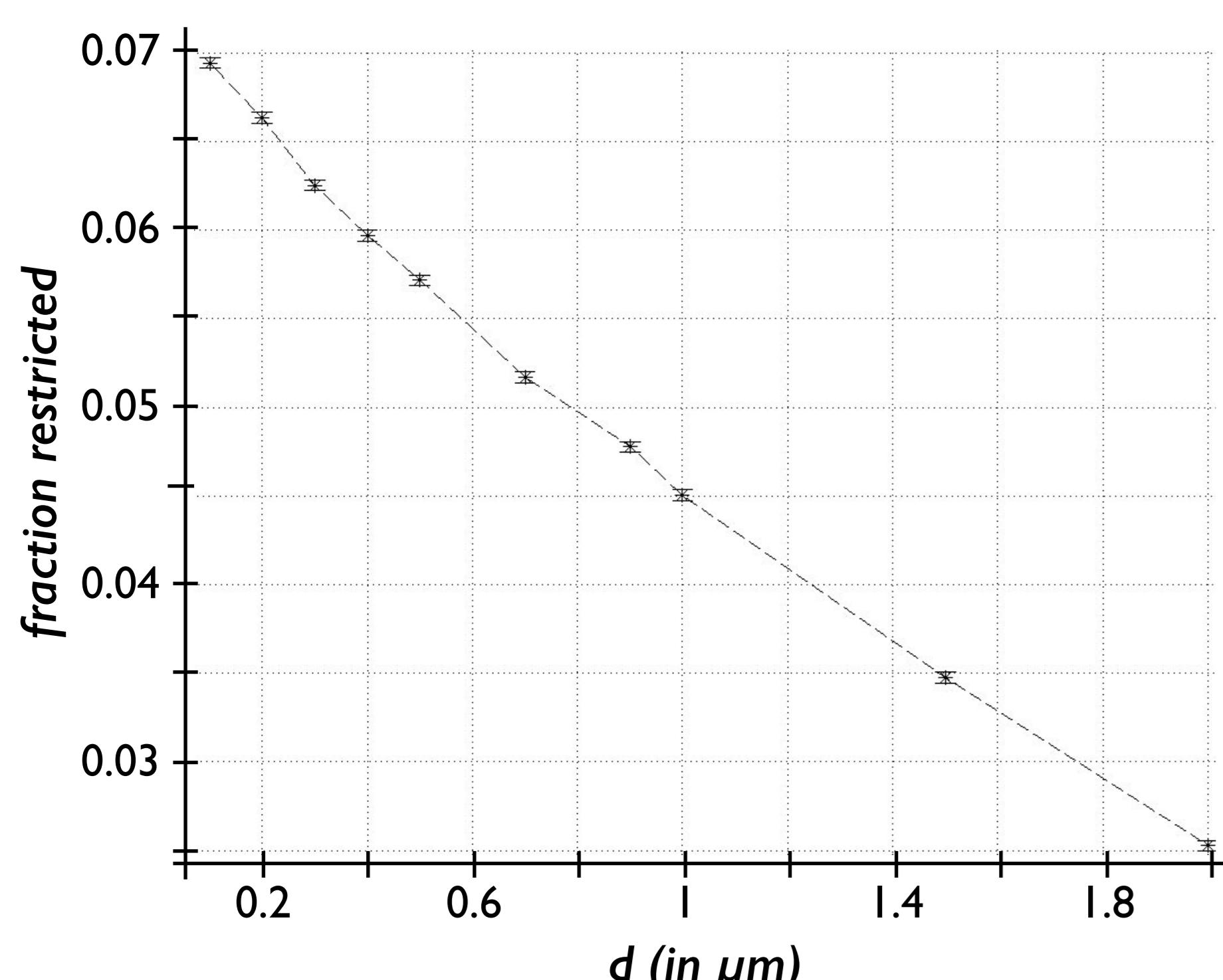
2



$\Phi_{\text{std}} < 0.003$ for the three cases when $\Phi_{\text{mean}} = 0.848/0.866$ for $\sigma=0.5/2.5$. Φ_{std} is lower than the variation's density in corpus callosum histology : $\Delta(\Phi)=0.01$ [5].

3

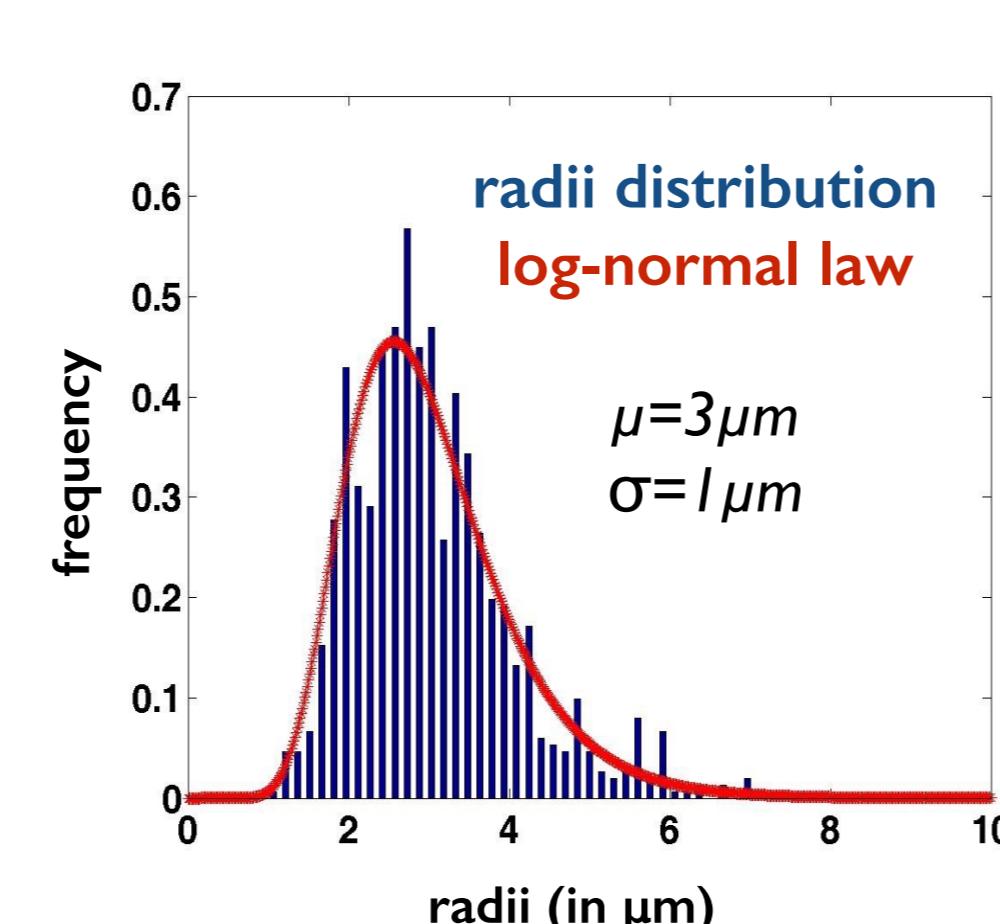
Range for fr



$d=0.1 \mu\text{m} \Phi=0.81$

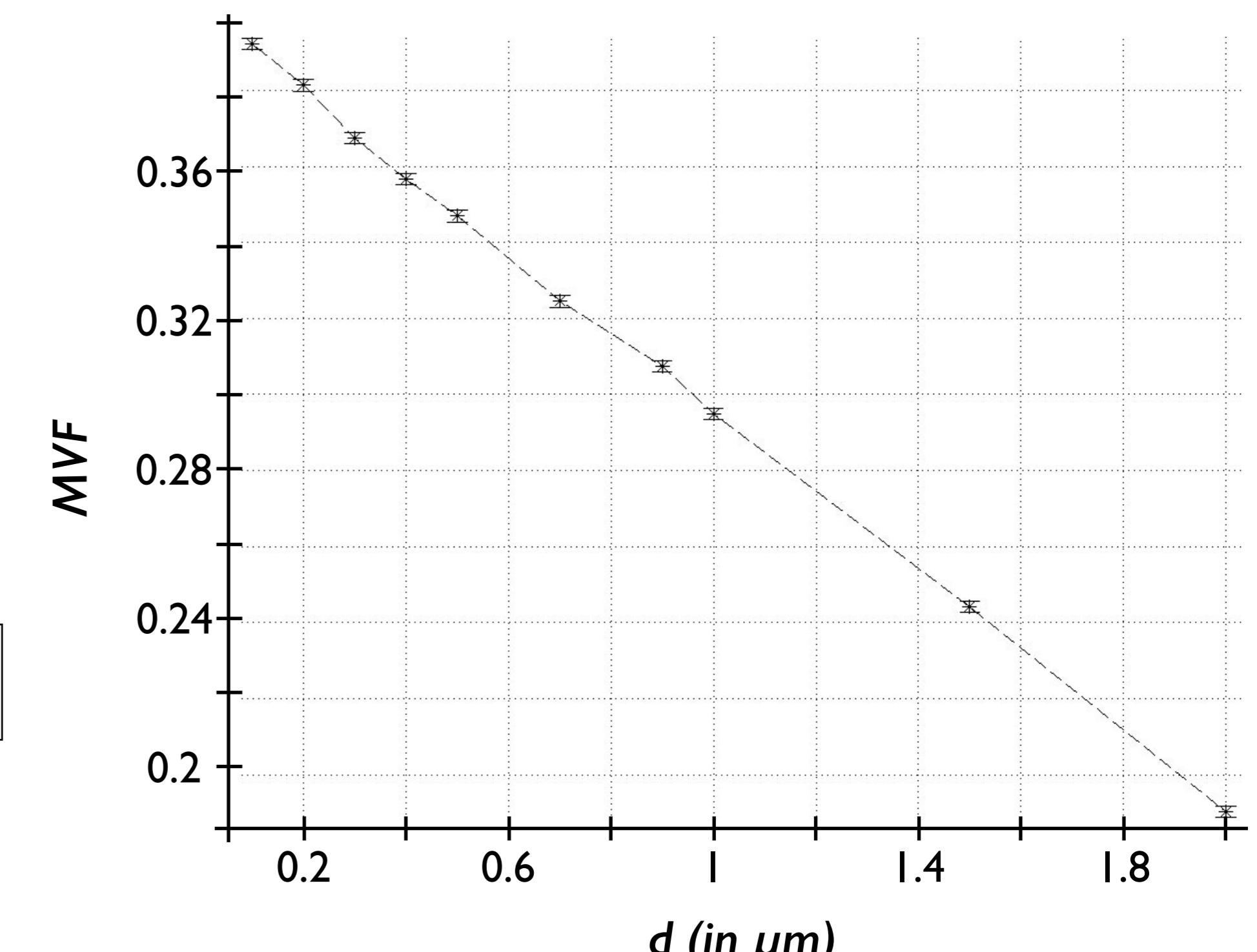
$d=1 \mu\text{m} \Phi=0.63$

$d=2 \mu\text{m} \Phi=0.49$



MVF ranged from 0.1 to 0.39.
fr ranged from 0.25 to 0.69.

Range for MVF



Conclusion

A new algorithm for the white matter simulation which accounts for the micro-structural features has been developed.

It has been validated by confronting a well-known mathematical case and by checking its reproducibility.

We could look at the evolution of fr and MVF when we fix the mean radii and vary the variance radii.

We expect this tool to be used for Monte-Carlo diffusion simulations or for extraction of fr and MVF on histological images by just measuring the gap and the radii distribution of axons.

Acknowledgements

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Contact: tom.mingasson@eleves.ec-nantes.fr

References

[1] Hall et al., 2008. [2] Sepehrband et al., 2016. [3] <https://goo.gl/dR1h9Q> [4] Meyer et al., 2010. [5] Stikov et al., 2009.