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Simulated Diffusion in Realistic Imaging Features of Tissue (Sim-DRIFT)

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Software

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Summary

This library, `simDRIFT`, provides for rapid and flexible Monte-Carlo simulations of Pulsed Gradient Spin Echo (PGSE) Diffusion-Weighted Magnetic Resonance Imaging (DWI) experiments, which we expect to be useful for DWI signal processing model development and validation purposes. The primary focus of this library is forward simulations of molecular self-diffusion processes within an ensemble of nuclear magnetic resonance (NMR) active nuclei ("spins") residing in complex, biophysical tissue systems. To achieve a large variety of tissue configurations, `simDRIFT` provides support for n fiber bundles (with user-defined radii, intrinsic diffusivities, orientation angles, and densities) and m cells (with user-defined radii and volume fractions). `simDrift` is written in Python (Python Software Foundation (VanRossum & Drake, 2010)) and supported by a Numba (Lam et al., 2015) backend. Thus, `simDRIFT` benefits from Numba's CUDA API, allowing the simulation of individual spin trajectories to be performed in parallel on single Graphics Processing Unit (GPU) threads. The resulting performance gains support `simDRIFT`'s aim to provide a customizable tool for the rapid prototyping of diffusion models, ground-truth model validation, and in silico phantom production.

Statement of need

Monte Carlo simulations are particularly effective at generating synthetic diffusion MRI data from complex, biophysically accurate imaging voxels with known ground-truth microstructural parameters. Consequently, such simulations have proven useful for developing and validating signal processing models (Chiang et al., 2014; Ye et al., 2020). Existing Monte Carlo simulators, such as CAMINO, Disimpy, Realistic Microstructure Simulator, and others, rely on meshes to discretize the computational domain (Ianuș et al., 2016; Kerkelä et al., 2020; Rafael-Patino et al., 2020; Yeh et al., 2013). While this approach does allow for the representation of complex and finely detailed microstructural features, given the coarse graining of such features (fiber bending, etc.) observed at experimentally realistic diffusion times and voxel sizes (Novikov et al., 2018), `simDRIFT` supplies a reasonable approximation to the relevant self-diffusion processes by parametrizing fibers as narrow cylinders, or "sticks", and cells as isotropic spheres, or "balls" (Behrens et al., 2003). This way, users may readily simulate voxels induced by multiple, oriented fiber bundles and cells without having to re-discretize the computational domain with complex meshes, which scale in size according to the desired feature resolution and size of the simulated image voxel (Panagiotaki et al., 2010).

`simDRIFT`'s superior computational performance represents an important advantage relative to other available open-source software. Comparisons between simDRIFT and Disimpy, a mesh-based, CUDA-enabled DWI forward simulator known to be faster than CAMINO (Kerkelä et al., 2020), on identical image voxel geometries featuring a 5 μm radius cell, reveals orders of magnitude improved performance, particularly for large resident spin ensemble sizes. Thus, `simDRIFT` is especially useful in a regime where the computational cost of existing software

may be cumbersome or even prohibitive. In particular, `simDRIFT` is able to perform large-scale simulations very quickly, therefore benefiting from favorable convergence properties with respect to the diffusion weighted signal. In this context, using just desktop- or even laptop-level GPU hardware, `simDRIFT` users are able to quickly and easily generate large amounts of synthetic DWI data from a wide variety of voxel geometries.

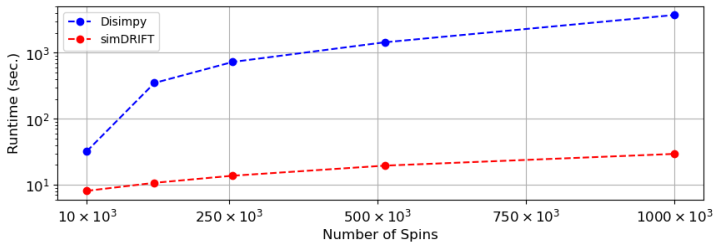

Figure 1: Runtime comparison between simDRIFT and Disimpy, another DWI simulator that runs on the GPU. These simulations were performed on a Windows 10 desktop with an Nvidia RTX 3090 GPU.

Therefore, the software encompassed by `simDRIFT` fulfills a presently-unmet need by allowing for mesh-free Monte Carlo simulations of DWI that unify researchers' needs for computational performance and biophysical realism with easy-to-use and configurable open-source software. `simDRIFT` was designed to be used by researchers of all disciplines and focuses on those who are working with diffusion MRI. Multiple scientific publications that utilize this library are currently in production. The wide customizability, high computational speed, and massively-parallel design will provide avenues for improved model development pipelines and thorough inter-model comparisons, among other potential applications.

Features

The library allows users to construct voxel geometries described by user-defined microstructural and scanning parameters. Specifically, `simDRIFT` simulates the diffusion MRI signal generated from the self-diffusion of water in an isotropic imaging voxel of length L_{voxel} that contains $n \in [0, 4]$ distinct fiber bundles and $m \in [0, 2]$ distinct cells types, according to the user's selection of diffusion imaging protocol, diffusion time (Δ), time-step size $\mathrm{d}t$, and desired free water diffusivity D_{FW}. Within each simulated voxel, the user also has control over the properties of each fiber/cell type. For each fiber bundle, users define the desired orientation (via the angle θ formed between the bundle and the z axis), intrinsic diffusivity (D_i), axonal radius (R_i), and voxel volume fraction V_i/V_{vox}. For each cell type, users similarly define the desired radius R_j and voxel volume fraction V_j/V_{vox}. Examples of such voxel configurations can be seen in 2.

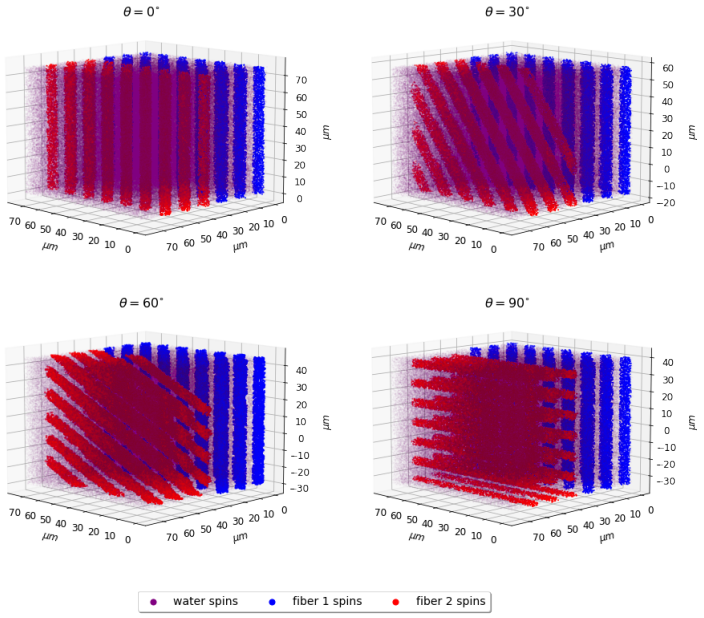

Figure 2: Example simulated spin trajectories from an imaging voxel featuring two fiber bundles (red, blue) with various orientations ($\theta = 0°$, 30°, 60°, 90°), along with extra-fiber spins (purple) .

For each time step $\mathrm{d}t$ in the simulation, each tissue compartment's resident spins are displaced along a randomly chosen direction with a compartment-dependent distance $\mathrm{d}L = \sqrt{6D_0\mathrm{d}t}$. This process is repeated until the target diffusion time of Δ is reached. For diffusion times shorter than the expected pre-exchange lifetime of intracellular water, it is safe to assume no exchange between tissue microstructures. The inter-compartmental exchange of water is computationally forbidden via within-timestep rejection of proposed moves beyond the boundaries of each spin's domain.

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References—

Behrens, T. E. J., Johansen-Berg, H., Woolrich, M. W., Smith, S. M., Wheeler-Kingshott, C. A. M., Boulby, P. A., Barker, G. J., Sillery, E. L., Sheehan, K., Ciccarelli, O., Thompson, A. J., Brady, J. M., & Matthews, P. M. (2003). Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. *Nature Neuroscience*, *6*(7), 750–757. https://doi.org/10.1038/nn1075

Chiang, C.-W., Wang, Y., Sun, P., Lin, T.-H., Trinkaus, K., Cross, A. H., & Song, S.-K. (2014). Quantifying white matter tract diffusion parameters in the presence of increased extra-fiber cellularity and vasogenic edema. *NeuroImage*, *101*, 310–319. https://doi.org/10.1016/j.neuroimage.2014.06.064

Ianuș, A., Drobnjak, I., & Alexander, D. C. (2016). Model-based estimation of microscopic anisotropy using diffusion MRI: A simulation study. *NMR in Biomedicine*, *29*(5), 672–685.

https://doi.org/10.1002/nbm.3496

Kerkelä, L., Nery, F., Hall, M., & Clark, C. (2020). Disimpy: A massively parallel Monte Carlo simulator for generating diffusion-weighted MRI data in Python. *Journal of Open Source Software*, *5*(52), 2527. https://doi.org/10.21105/joss.02527

Lam, S. K., Pitrou, A., & Seibert, S. (2015). Numba: A LLVM-based Python JIT compiler. *Proceedings of the Second Workshop on the LLVM Compiler Infrastructure in HPC*, 1–6.

Novikov, D. S., Kiselev, V. G., & Jespersen, S. N. (2018). On modeling. *Magnetic Resonance in Medicine*, *79*(6), 3172–3193. https://doi.org/10.1002/mrm.27101

Panagiotaki, E., Hall, M. G., Zhang, H., Siow, B., Lythgoe, M. F., & Alexander, D. C. (2010). High-fidelity meshes from tissue samples for diffusion MRI simulations. In *Medical image computing and computer-assisted intervention – MICCAI 2010* (pp. 404–411). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-15745-5_50

Rafael-Patino, J., Romascano, D., Ramirez-Manzanares, A., Canales-Rodríguez, E. J., Girard, G., & Thiran, J.-P. (2020). Robust Monte-Carlo simulations in diffusion-MRI: Effect of the substrate complexity and parameter choice on the reproducibility of results. *Frontiers in Neuroinformatics*, *14*. https://doi.org/10.3389/fninf.2020.00008

VanRossum, G., & Drake, F. L. (2010). *Python language reference manual*. Python software foundation Amsterdam, Netherlands.

Ye, Z., Gary, S. E., Sun, P., Mustafi, S. M., Glenn, G. R., Yeh, F.-C., Merisaari, H., Song, C., Yang, R., Huang, G.-S., Kao, H.-W., Lin, C.-Y., Wu, Y.-C., Jensen, J. H., & Song, S.-K. (2020). The impact of edema and fiber crossing on diffusion MRI metrics assessed in an ex vivo nerve phantom: Multi-tensor model vs. diffusion orientation distribution function. *NMR in Biomedicine*, *34*(1). https://doi.org/10.1002/nbm.4414

Yeh, C.-H., Schmitt, B., Bihan, D. L., Li-Schlittgen, J.-R., Lin, C.-P., & Poupon, C. (2013). Diffusion microscopist simulator: A general Monte Carlo simulation system for diffusion magnetic resonance imaging. *PLoS ONE*, *8*(10), e76626. https://doi.org/10.1371/journal.pone.0076626