



# INTELLIGENT SYSTEMS ENGINEERING

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INDIANA UNIVERSITY  
School of Informatics, Computing, and Engineering

Dear Editor of Science Advances,

5/1/2020

We are submitting the article entitled “Separable homological optimization for intravoxel incoherent motion”.

The article provides multiple innovations which will be beneficial across the domains of science, engineering and medicine.

First, we identify a crucial problem in medical imaging. A recently FDA approved biophysical model for MRI imaging analysis known as IVIM (intravoxel incoherent motion) is becoming more and more popular (2000+ publications since 2016) . However, scientists and MDs are undermining the difficulty of fitting this model to the data although concerns have been raised in the diffusion microstructure community. The model is extremely hard to fit and all existing optimization solutions are providing erroneous maps that do not represent the underlying anatomy. As IVIM is being used as a biomarker for tumor detection or other disorders, incorrect optimization could lead to misleading diagnosis. Secondly, the IVIM model although simple and having a few parameters to fit is highly nonlinear and can have multiple global minima. This is a problem that most existing optimization schemes cannot resolve in general as they assume a single global optimum.

For the above reasons we created a new method that we call TopoPro that can resolve the parameters of the IVIM model and can be used also to study the topological subdomains of the objective function. Our results show that we outperform the pre-existing methods 10X in finding the correct parameters. Our solutions are stable and have no fluctuations which is a major problem with the currently available techniques. To resolve this problem was definitely not easy as we had to build a new method that takes ideas from homology, a field of topology not commonly used for optimization, and separable nonlinear optimization with variable projection, also known as VarPro.

TopoPro, our proposed method, is a tool that is currently missing from the community as there is no robust method that can reliably fit the IVIM model. Therefore we have decided to provide it freely in DIPY which is the most popular diffusion imaging software in Python. Note that DIPY has more than 100 contributors on



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GitHub which is rare for medical imaging software. Therefore, having such a community will help reach out to the scientists that have to improve their analysis methods.

The code is publicly available, open access and the data used are also publicly available. Software at all levels from interfaces, to Python scripts and to Jupyter notebooks have been developed in support of this paper.

Finally, we have no reason to believe that this framework will not be able to be applied to other models. The method is generic (derivative free optimization) and can be used in other models inside or outside the world of MR. Therefore, we believe that Science Advances is the right venue for this work as the method proposed has a broad impact and it mitigates a vital issue by leveraging state-of-the-art developments in mathematical optimization and algebraic topology.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Eleftherios'.

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