

LETTER TO THE EDITOR

Reply: Computer models to inform epilepsy surgery strategies: prediction of postoperative outcome

Nishant Sinha,^{1,2} Justin Dauwels,³ Marcus Kaiser,^{1,2} Sydney S. Cash,⁴ M. Brandon Westover,⁴ Yujiang Wang¹ and Peter N. Taylor^{1,2,5}

1 ICOS, School of Computing Science, Newcastle University, UK

2 Institute of Neuroscience, Newcastle University, UK

3 School of Electrical and Electronic Engineering, Nanyang Technological University, Singapore

4 Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

5 Institute of Neurology, University College London, UK

Correspondence to: Peter N. Taylor

ICOS, School of Computing Science, Newcastle University, UK

E-mail: peter.taylor@newcastle.ac.uk

Sir,

We are encouraged that Goodfellow and colleagues (2016) found similar results to ourselves (Sinha *et al.*, 2017). Indeed, both studies follow our review where we proposed computational modelling of epilepsy surgery (Taylor *et al.*, 2014), and our earlier work where we suggested alternative resection strategies based on our model simulations (Sinha *et al.*, 2014; Hutchings *et al.*, 2015). Other groups have also made valuable contributions in this area (Proix *et al.*, 2016). A key principle to understand in the above studies, is that the parameters of the computer models are constrained and determined by the patient-specific networks—in our case functional networks measured using intracranial EEG. This data-constrained modelling approach has shown promise, so far in small cohorts of patients. Here, we will discuss some limitations and suggest future directions.

As a consequence of using intracranial recordings, an important limitation of both studies is the incomplete nature of the data underpinning the model. In particular, there is a lack of spatial coverage since only a part of the brain is covered by the recording electrodes. MEG recordings could be one way of mitigating this problem. One elegant study by Englot and colleagues (2015) used source localized MEG recordings of interictal activity. Although a computer model was not used in that study, the authors did investigate network properties, which would influence our model outputs. A second way of

improving spatial coverage could be to use functional MRI. For example, it has already been shown using concurrent EEG-fMRI how interictal epileptiform discharges can be used for predicting surgery outcome (Coan *et al.*, 2016).

Another way to improve on both our studies may be to include data from other sources to further constrain computer model parameters. For example, structural networks, such as those measured by diffusion imaging, may be useful for predicting outcome (Bonilha *et al.*, 2013; Munsell *et al.*, 2015). It is unclear, however, how predictions based on structural networks relate to predictions made on functional networks in the same patient. Computer models offer an ideal tool to investigate this relationship. We agree that, although not entirely removing human bias due to manual segmentation, using pre- and postoperative MRI to delineate resection area, as in Goodfellow *et al.*, is a positive step in this direction of multimodal data integration. Moving forward, integrating multimodal data using computer models could negate the drawback of the currently limited spatial coverage of intracranial recordings in both studies, in addition to unifying current literature.

Further unification of current literature could be performed using a computational model, for example, to understand seizure spreading patterns in addition to predicting surgical outcomes (Jirsa *et al.*, 2017). Our use of ‘escape time’, which is the time a brain region (network node) takes to transition to the seizure state in the model,

may serve as an excellent way to investigate the underlying mechanisms of seizure genesis and evolution.

Finally, to make progress in the field of surgery outcome prediction, we can perhaps learn important lessons from the field of seizure prediction. A major issue in the early days of seizure prediction was that many studies were based on limited sample sizes, heterogeneous data, and over fitted models (Freestone *et al.*, 2015). This made the studies difficult to compare to each other, and translation into clinical use was hindered. Similar problems exist in our case of surgery outcome prediction. Low subject numbers, inconsistent follow-up time, and heterogeneous patient cohorts make comparison between studies difficult. For example, the study of Goodfellow *et al.* and our study both only had 16 subjects. Goodfellow *et al.* mainly included temporal lobe patients with magnetic resonance visible lesions, whereas the majority of our subjects were extra-temporal non-lesional patients. Despite this, and despite using different underlying data (ictal versus interictal), we find it encouraging that both studies independently come to similar conclusions.

The approach of data driven modelling holds promise for developing patient-specific treatment strategies. We hope that in future, multimodal data integration and systematic comparisons of models, measures, and modalities on larger cohorts will move the field forward.

References

Bonilha L, Helpert JA, Sainju R, Nesland T, Edwards JC, Glazier SS, et al. Presurgical connectome and postsurgical seizure control in temporal lobe epilepsy. *Neurology* 2013; 81: 1704–10.

- Coan AC, Chaudhary UJ, Grouiller Frédéric, Campos BM, Perani S, De Ciantis A, et al. EEG-fMRI in the presurgical evaluation of temporal lobe epilepsy. *J Neurol Neurosurg Psychiatry* 2016; 87: 642–9.
- Englot DJ, Hinkley LB, Kort NS, Imber BS, Mizuiri D, Honma SM, et al. Global and regional functional connectivity maps of neural oscillations in focal epilepsy. *Brain* 2015; 138: 2249–62.
- Goodfellow M, Rummel C, Abela E, Richardson MP, Schindler K, Terry JR. Estimation of brain network ictogenicity predicts outcome from epilepsy surgery. *Sci Rep* 2016; 6: 29215.
- Freestone DR, Karoly PJ, Peterson AD, Kuhlmann L, Lai A, Goodarzy F, et al. Seizure prediction: science fiction or soon to become reality? *Curr Neurol Neurosci Rep* 2015; 15: 73.
- Hutchings F, Han CE, Keller SS, Weber B, Taylor PN, Kaiser M. Predicting surgery targets in temporal lobe epilepsy through structural connectome based simulations. *PLoS Comput Biol* 2015; 11: e1004642.
- Jirsa VK, Proix T, Perdakis D, Woodman MM, Wang H, Gonzalez-Martinez J, et al. The virtual epileptic patient: individualized whole-brain models of epilepsy spread. *Neuroimage* 2017; 145: 377–88.
- Munsell BC, Wee CY, Keller SS, Weber B, Elger C, da Silva LA, et al. Evaluation of machine learning algorithms for treatment outcome prediction in patients with epilepsy based on structural connectome data. *Neuroimage* 2015; 118: 219–30.
- Proix T, Bartolomei F, Guye M, Jirsa VK. Individual brain structure and modelling predict seizure propagation. *Brain* 2017; 140: 641–54.
- Sinha N, Dauwels J, Wang Y, Cash SS, Taylor PN. An in silico approach for pre-surgical evaluation of an epileptic cortex. In: Engineering in Medicine and Biology Society (EMBC), 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE. 4884–4887, <http://ieeexplore.ieee.org/document/6944718/>, <https://doi.org/10.1109/EMBC.2014.6944718>.
- Sinha N, Dauwels J, Kaiser M, Cash SS, Brandon Westover M, Wang Y, et al. Predicting neurosurgical outcomes in focal epilepsy patients using computational modelling. *Brain* 2017; 140: 319–32.
- Taylor PN, Kaiser M, Dauwels J. Structural connectivity based whole brain modelling in epilepsy. *J Neurosci Methods* 2014; 236: 51–7.