Lift-Off Fellowship report: Making the methods – and the case – for discerning useful models prior to the collection of biomolecular interaction data

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The support provided by an AustMS Lift-Off Fellowship allowed me to pursue some matters noted, but not substantially explored, in my PhD thesis: 'Global *a priori* identifiability of flow-cell optical biosensor experiments'.

My PhD research related to inverse problems arising in the study of biomolecular interactions by use of a particular, widely used apparatus. My specific interest lay in determining whether one may expect to obtain a unique estimate of each parameter (rate constant) from an idealised data record that is infinite in extent and error free. If so, then the model has the property of (global *a priori*) identifiability. A negative outcome suggests that we are unlikely to obtain a unique estimate of a parameter vector from real, noisy data. This is problematic if we are unable to distinguish between alternative, equally valid, parameter vectors.

Ideally, we apply a test in advance of data collection. A negative result allows us to anticipate an uninformative study outcome. This indicates some undesirable feature in the combination of planned experiments and assumed mathematical model. Further, the test may provide insight on how to modify this in order to arrive at a study more likely to achieve a definitive result.

My thesis focused mostly on analytical methods for testing an assumed model for identifiability. However, the models found in the literature may have undeclared assumptions, or occur in a variety of forms that are not readily comparable. This is an impediment to their understanding and analysis.

The Lift-Off Fellowship gave me the time and opportunity to address this issue. In particular, I proposed a framework for specifying models unambiguously. I used this to completely specify a commonly used model and compare this to alternative forms seen in the literature. This will provide a concrete example of how an alternative form of a model can have properties that are more desirable than those of the original.

I have prepared manuscripts relating to both the general framework ([1]) and specific model representation ([2]). I intend to submit these to suitable journals in the near future. To accompany the manuscripts, I am refining a web app made using the R package Shiny ([3]). This app will use user-supplied parameter values

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to generate output from a particular model, and return different parameter values that produce the same output. The intent of this is to assist a non-mathematical audience appreciate the benefits of my research.

I expect the research undertaken as a Lift-Off Fellow will have two main results. The first is raising awareness in the biosensor community of the usefulness of scrutinising properties of an assumed model. The second is an easier path to specifying further test cases for the analytical methods proposed in my thesis.

References

[1] Whyte, J.M. The practical value of an explicit response model in quantitative uses of Biacore^{TM} biosensors. In preparation.
[2] Whyte, J.M. Resolving ambiguity in models of SPR biosensor data featuring the 'simple bimolecular interaction'. In preparation.
[3] Whyte, J.M. An illustration of parameter value non-uniqueness for a four-parameter model of Biacore biosensor data subject to the 'simple bimolecular interaction' (working title). In preparation.

Jason studied at The University of Adelaide for his B.Sc. (Science), B.Sc. (First Class Hons, Mathematical and Computer Sciences), and The Amir Hasan Abdi Prize (co-recipient). Adelaide-era roles included Technical Editor of the ANZIAM Journal during the tenure of his Ph.D. supervisor Professor C.E.M. Pearce, and Research Associate on an ARC discovery project. He completed his Ph.D. in the School of Mathematics and Statistics at The University of Melbourne, supervised by Professors Tony Guttmann and Peter Taylor. He is an Associate Investigator of ACEMS, and recently commenced Postdoctoral Research Fellow at the Centre of Excellence for Biosecurity Risk Analysis (CEBRA).