

# Everything Changes Over Time: Transforming Joint Modelling Methodology

*supervised by*

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Clinicians typically collect data from patients regularly throughout the treatment of an illness. Such longitudinal data provides valuable insights into how things change over time for patients tracking the progression of the disease, a patient's reaction to particular treatments, the usefulness of intervention strategies, for example. It is common that such data will be collected alongside key event information such as the time to recovery, time to relapse or time to death of patients. Joint models enable the relationships between this survival and longitudinal data to be mathematically represented, frequently linking a linear mixed effects model to a Cox proportional hazards model [1, 2].

Despite the significant growth in this field of research in recent years, a wider array of models is needed to truly represent natural biological changes over time. With joint models being first introduced in 1996, this relatively young field of research has many opportunities in which novel approaches can be explored. This project will tackle one such avenue of research – the transformation of joint modelling methodology to allow a better representation of changing effects over time.

Within current literature, joint models assume that the effect of covariates is constant, unchanging over time, a potentially unrealistic assumption which this research would relax. By lending theory from time-varying parameter models [3], this project would take into account the likely situation that as a disease progresses, the relationship between the response and covariates (e.g. biomarkers or drug effects) tend to strengthen and change over time. Examples of this are given within many medical fields such as the analysis of biomarkers associated with Parkinson's disease, antiviral treatment effects for HIV patients and the analysis of people trying to quit smoking, to name but a few.

This PhD would feed into a user-friendly software package, complementing other active research projects currently being undertaken by the primary supervisor in conjunction with both national and international collaborators.

## REFERENCES

- [1] WULFSOHN, M.S. & TSIATIS, A Joint Model for Survival and Longitudinal Data Measured with Error, *Biometrics* 1997;53(1):330-339.
- [2] IBRAHIM, J.G., CHU, H. & CHEN, L.M., Basic Concepts and Methods for Joint Models of Longitudinal and Survival Data, *Journal of Clinical Oncology* 2010;28(16):2796-2801.
- [3] KOOPMAN, S.J, LUCAS, A. & SCHARTH, M., Predicting time-varying parameters with parameter-driven and observation-driven models, *Review of Economics and Statistics* 2016;98(1):97-110.