Department of Pathology fully-funded PhD studentships: project proposal form

PIs to complete Parts A & B and to send to your Head of Division by 1 November 2020.
Heads of Division to complete Part C and to send to hod.sec@path.cam.ac.uk

PART A: PROJECT PROPOSAL	
Division	CMP
Supervisor	Michael Boemo
Second supervisor (If supervisor's contract ends before October 2025)	Anton Enright
Project title	Computational methods to measure DNA replication with single-molecule resolution
Project abstract for advert (Max 100 words)	In the time it takes you to read this sentence, your body will produce millions of new cells. It is critical that each of them replicated their DNA accurately; errors in DNA replication can lead to cancer. The Boemo Group is a computational biology laboratory developing artificial intelligence software that measures the movement of replication forks from Oxford Nanopore sequencing data. The student will develop novel algorithms and computational approaches to track the movement of replication forks in both human cells and infectious microorganisms and develop cutting-edge mathematical models that can be used to predict targets for replication-based therapies.
Keywords Please provide up to five	DNA replication; machine learning; computational biology; genome stability; nanopore sequencing
Full details (Max 250 words) **Will be published on Departmental website; please do not include confidential information**	In the time it takes you to read this sentence, your body will produce millions of new cells. It is critical that each of them replicated their DNA accurately; errors in DNA replication can lead to genome instability and cancer. Cancerous cells often show different patterns of replication compared with healthy human cells, making DNA replication an important therapeutic target. However, studying DNA replication at scale is a challenging problem: Existing methods either measure how a population of cells replicate, which "averages out" rare but important behaviour,

	or they work with single-molecule resolution but have low throughput. The Boemo Group is a computational biology laboratory developing artificial intelligence software that measures the movement of replication forks from Oxford Nanopore sequencing data. This method provides a high-throughput, inexpensive, accurate, and automated way to measure replication fork movement. The student will develop novel algorithms and computational approaches to track the movement of replication forks in both human cells and infectious microorganisms. The student will also develop cutting-edge mathematical models of DNA replication that can be used to predict targets for replication-based therapies. This project will be highly collaborative with different laboratories around the world, and there will be the opportunity to learn, or improve upon, software engineering in Python/C/C++, GPU computing, deep learning with TensorFlow, the processing and management of large datasets.
Three of your most important publications in support of the proposed project	Mueller, C.A., Boemo, M.A., Spingardi, P., Kessler, B. Kriaucionis, S. Simpson, J.T., Nieduszynski, C.A. (2019) Capturing the dynamics of genome replication on individual ultra-long nanopore sequencing reads. *Nature Methods* 16:429-436. Boemo, M.A., Cardelli, L., Nieduszynski, C.A. (2020) The Beacon Calculus: A formal method for the flexible and concise modelling of biological systems. *PLoS Computational Biology* 16:e1007651. Boemo, M.A. (2020) DNAscent v2: Detecting replication forks in nanopore sequencing data with deep learning. *bioRxiv*.