How do bones acquire their shapes? Establishing a paradigm for the biology and mechanobiology of morphogenesis of synovial joints.

Supervisors: Dr Niamh Nowlan, Department of Bioengineering, Imperial College London
Dr Chrissy Hammond, School of Physiology, Pharmacology and Neuroscience, University of Bristol

The movement of a baby in the womb is critical for normal development of their bones and joints, but the link between the mechanical stresses and strains that arise due to these movements and critical processes during formation of the skeleton remains unclear. This is due to the complex interactions that occur between biological (cell activity) and mechanical influences (stresses and strains) as the skeleton forms. In this proposal, we will combine experimental and computational modelling techniques to reveal the 'rules' governing prenatal joint development.

The types of questions that we plan to answer include:
When, with what direction, and where in the joint do cells divide in order to bring about shape change?
How are these aspects of cell activity affected by a chance in the mechanical environment?
What are the stresses and strains induced in the developing joint by fetal movements?
How do these stresses and strains affect cell activity?
Obtaining the data to answer these questions, and then (crucially) integrating the different types of data in a computational simulation of the process of joint development will bring about a step change in our understanding of how our joints form.

We will use fish and chick models to gather information on how joint shapes and patterns of cell activity are affected by a change in the fetal movements. We will then incorporate these data into a computational model which (at the end of the project) will be able to predict how joints grow and change in shape over development.

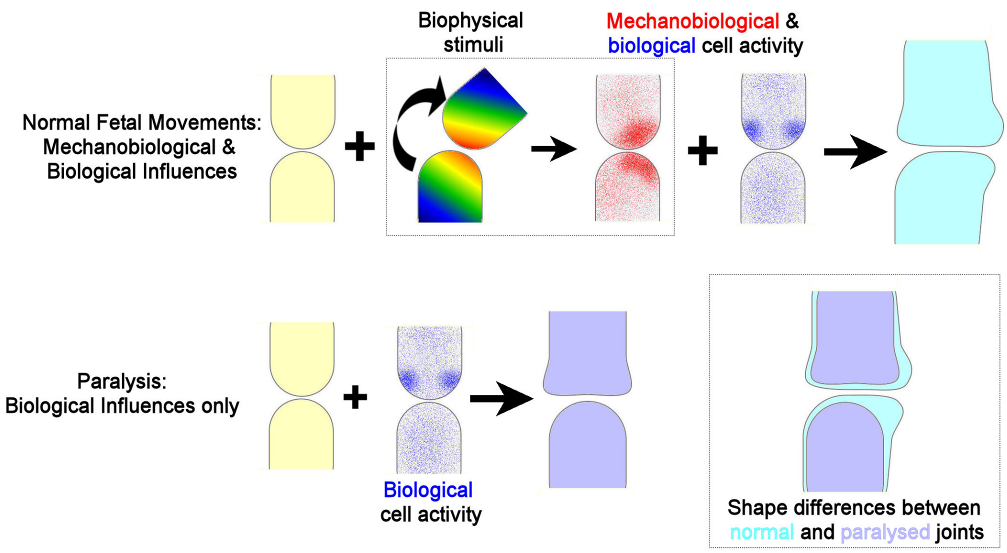

Figure 1: Joint morphogenesis is determined by the former shape and the combined influences of biological and mechanobiological factors. Biological factors can be isolated by eliminating fetal movements, but mechanobiological activity is impossible to isolate. This proposal will unravel the complex relationship between these influences to define a unified paradigm for joint morphogenesis.