The lay summary is a brief summary intended to facilitate knowledge transfer and enhance accessibility, therefore the language used should be non-technical and suitable for a general audience. (See the Degree Regulations and Programmes of Study, General Postgraduate Degree Programme Regulations. These regulations are available via: <http://www.drps.ed.ac.uk/>.)

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| Title of thesis: | Unravelling higher order chromatin organisation through statistical analysis | | | |

Insert the lay summary text here - the space will expand as you type. Your lay summary must be contained on this side.

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| Each human cell contains DNA that would extend for two metres if fully straightened. Instead, this length of DNA is highly compacted into micrometre-sized cell nuclei. Recently experimental methods such as Hi-C have been developed which allow the inspection of this folded state, generating counts of how frequently chromosomal regions are interacting with each other. These counts can be statistically analysed to reveal different levels of structures, including loops between two distant locations, knot-like domains of self-interacting regions, and broad stretches of mostly active or inactive regions.  In this work, we bring together Hi-C datasets from several different publications and combine these with a large number of chromatin datasets that quantify, for example, levels different DNA-binding proteins as well as modifications to DNA packing histone proteins. We used these datasets to build predictive models of active and inactive states across each human chromosome in three different cell types, and achieved high predictive accuracy. We then compare and contrast these models, and use them to identify the key features which define active and inactive states.  We also analyse the boundaries between domains and compare these across cell types. We find the domains themselves are highly conserved between cell types, but observe different chromatin features marking domain boundaries. Further collaborative work involved analysis of boundaries from Hi-C data taken over successive time points, where boundary markings were found to persist as cells differentiate from stem cells.  Overall we find the three-dimensional DNA structures within cells are highly similar even between human embryonic stem cells and cells derived from blood. Where there are differences, these areas tend to highlight biological activity specific to that cell type. |