Omics data integration with genome-scale modelling of dopaminergic neuronal metabolism

Parkinson's disease is the second most common neurodegenerative disease in the world. One of its symptoms is the loss of dopaminergic neurons in the substantia nigra pars compacta. A number of phenotypes, including the aggregation of misfolded proteins, mitochondrial dysfunction, and neuroinflammatory chemicals released by microglia and activated astrocytes, may all play a role in its pathogenesis.

Due to the multisystemic nature of Parkinson's disease, novel tools for developing mechanistic models that simulate its pathogenic processes have been proposed. Furthermore, as the amount of information in biological databases grows and the cost of multi-omic experiments decreases, methods for integrating different types of biological data have become essential for increasing the level of detail in mechanistic models of biological systems.

Constraint-based modelling is a valuable tool in bioengineering and biomedicine. It is used to estimate the reaction flux in a metabolic network. The constraints represent essential characteristics of a biological system, including connectivity between metabolites and reactions, thermodynamics, maximum and minimum flux rates, and the steady-state.

This thesis presents studies and tools for integrating various types of specific information to genome-scale models used in constraint-based modelling. In addition, is presented the `iDopaNeuro` models, genome-scale models of a culture of dopaminergic neurons derived from induced pluripotent stem cells.