Description of Masters Project:

Central to all neuronal functions are the trillions of chemical synapses within the human brain that transmit chemical signals. This process is performed and regulated by complex protein networks in the pre- and post- synaptic termini. In the past efforts in synaptic-proteomics have been focused on identifying the constituents of the synaptic sub-compartments. Over 2000 gene products have been identified, but their binary interactions have not previously been studied on a large scale. To gain more insight into multi-protein complexes formed at the synapse we have adopted a high-throughput screening strategy; approximately 1000 proteins are being tested for pair wise interaction using the yeast-2-hybrid technique [5].

Following Y2H screening, selection of interacting protein pairs for validation will be based upon a scoring system which takes into account six factors: 1) known interactions between orthologues, 2) the presence of domains known to interact in each of the proteins, 3) co-expression, 4) co-localisation, 5) participation in the same biological process and 6) distance in an interaction network made up of all known interactions. High confidence interactions will be validated using the Lumier method [1], in which the interacting proteins are transiently co-expressed and then co-immunoprecipitated.

We now require a master student who can help us analyse the large-datasets produced by the LUMIER assay and integrate these results with our Y2H data. We hope to use this analysis to make predictions regarding protein localisation and function. The protein interaction network generated by this study will be a useful tool for studies on synapse dysfunction, which is central to the etiology and progression of several neurological disorders including neurodegeneration, autism and schizophrenia.