principles greatly facilitates integration, transformation and analysis of the data in a uniform format while keeping data in different layers according to their sources. The non-overlapping portions of the layers can be used to suggest new interactions, which might not have been detected by a particular type of experiment but highlighted in several others.

The aim of our work is to develop a model capable of predicting missing information in PPI network of a given pathway from different available data of multiple types. To this end, it is necessary to start by assembling a Boolean model of the selected pathway using literature research findings. The core model will then be expanded by addition of new links to the network structure based on suggested connections from different layers of data. We will also devise a formal model by specifying the rules of PPI in order to filter validate whether the asserted interactions are viable.

By applying this method, we will attempt to devise and complete the model for mitogen-activated protein kinase (MAPK) PPI network. MAPK network is a very well studied pathway and misregulated in various types of cancer. MAPK pathways are highly conserved pathways involve in regulation of various processes such as apoptosis, survival, growth, differentiation and migration in cell and disruption of each may lead to formation of tumor cells. Their role in directing growth factor and mitogens is of particular interest in cancer studies. As such, our main focus will be on the role of critical elements involved in regulating these pathways. Our ultimate aim is to build a network structure based on available PPI knowledge and compare the network with the network built from experimental data in order to predict the missing information in the network topology.

References:

P42: Footprinting Microbial Metabolites in Nature and Medicine
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The study of metabolic alterations in response to genetic and environmental perturbations has been a central topic in microbial metabolomics (Fiehn, 2002; Kol et al., 2010; Villas-Boas et al., 2008). Some of these alterations can be readily detected by changes in their surroundings, normally associated with metabolites that are released by cells as by-products of the metabolism or as extracellular signalling molecules to mediate cross-talk within microbial communities. The analysis of these metabolites, also known as metabolic footprinting, has been widely applied with different purposes: discriminating between metabolic phenotypes in order to classify and identify mutant strains (Villas-Boas et al., 2008); monitoring bioprocesses with the aim to detect specific metabolites that indicate alterations in the culture performance (Carneiro et al., 2011; Sue et al., 2011); and identifying quorum-sensing metabolites that indicate potential targets to annihilate pathogens (Birkenstock et al., 2012). These metabolic readouts have been also useful to give insights into intracellular metabolic activities and provide a straightforward way to analyse simultaneously multiple metabolic activities, since no extraction procedures are required to analyse the endometabolome (i.e., intracellular metabolites).
Thus, through metabolic footprint analysis we can assess central metabolic activities that characterize the reproduction and survival of organisms.

We have developed a methodology to evaluate the metabolic state of microbial cultures by analysing the footprints of two microbial systems: the bacterium *Escherichia coli* and the human pathogen *Helicobacter pylori* that increases the risk of gastric cancer. Strategies for sampling and sample preparation were developed, as well as the analytical procedures based on gas chromatography with mass spectrometry (GC-MS). A wide variety of metabolites was detected, including fatty, amino and organic acids, which allowed us to address changes in most central metabolic pathways, such as the tricarboxylic acid cycle (TCA cycle), the biosynthesis of amino and fatty acids, as well as other energy generating metabolic reactions.

The analysis of extracellular metabolites of *E. coli* cultures at different growth conditions were first performed to discriminate the physiological state of cultures and to evaluate the metabolic alterations produced at different growth conditions. According to our results in these experiments, metabolic footprints are good indicators of alterations in the intracellular metabolism. Next, the metabolic footprints of *H. pylori* cultures were investigated to get insights on the catabolism of this human pathogen. Overall, fifteen amino acids were detected in extracellular medium; six of them were confirmed as essentials for *H. pylori* growth, four amino acids were identified as non-essentials and can be used as carbon source, whilst five amino acids were identified as non-essentials and non-carbon source. In addition, some organic acids were also identified as carbon sources for *H. pylori*. This metabolic footprint analysis of *H. pylori* cultures allowed us to uncover key metabolic activities, mainly related with amino acids catabolism and to get insight on the metabolic behaviour of this organism.

The characterization of catabolic pathways, as well as of possible metabolic constraints, is of major importance to understand the dynamic basis of the interactions host–microbe in the human gut, and in particular to discover potential ‘diagnostic’ biomarkers. It is well-known that pathogen’s metabolism can influence the host health and may affect drug metabolism, toxicity and the efficacy of therapies (Holmes et al., 2011). However, little is known about their metabolic structure and behaviour. Our methodology allows uncovering part of the metabolic structure of *H. pylori* metabolism and undisclosed catabolic activities.

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References:
Deregulations of signalling pathways are known to be involved in the emergence and progression of cancers. Reductionist approaches over the last few decades have provided us with good understanding of the main mechanistic steps in many pathways, which are traditionally viewed as cascades of events that translate a ligand-mediated extracellular signal into phenotypic outcomes. In reality, however, a ligand can trigger multiple pathways and multiple ligands can trigger overlapping pathways via feedback and crosstalk interactions which operate by means of transcriptional and non-transcriptional mechanisms. It is through these complex, integrated networks of signalling pathways that cells process and make fate-related decisions, rendering it difficult to dissect the contribution to phenotypic outcomes of different extracellular signals.

To gain further understanding of how different signalling pathways exchange information to translate multiple extracellular signals into cellular phenotypes, we are developing a large-scale computational model which integrates many well-known signalling pathways, such as the MAPK/ERK pathway, PI3K/AKT pathway, JAK/STAT pathway, p53/Mdm2 pathway, and the Caspase signalling pathway. These pathways are triggered by a variety of stimuli such as the Epidermal Growth Factor (EGF), Cytokines, Insulin and Tumor Necrosis Factor (TNF), and lead to a wide range of phenotypic outcomes such as proliferation, differentiation, cell division, adhesion and apoptosis.

Complex diseases such as cancers often result from multiple mutations, many of which occur in the pathways considered in our computational model. Our large-scale model, therefore, has the potential to reveal how carcinogenic mutations modulate the signalling mechanisms and cause inappropriate cellular phenotypes which may lead to tumour development. This information can then be used to pinpoint parts of the signalling mechanisms that can be targeted for more efficient cancer therapy. The model would also be a valuable tool to explore novel therapies where combinations of different drugs are used to target multiple molecules.

**P44: Analysis of the mTOR/DEPTOR signalling system reveals a novel mechanism of oscillations based on protein-protein interactions**

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Background: The mammalian target of rapamycin (mTOR) signalling pathway plays central roles in the control of cell survival, proliferation and tumourogenesis. Recently, DEPTOR has been identified as a new mTOR-interacting protein whose degradation is mediated by both mTORC complexes (mTORC1/2). Their interplay endows the mTOR pathway with intricate interlinked feedback mechanisms capable of