Visualisation of the Complexome

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Introduction

- Proteins and other molecules interact with each other to form macromolecular complexes, which are the functional units inside the cell. Together, these make up the complexome.

- To date, there are 4 large-scale datasets for protein complexes in *Saccharomyces cerevisiae*. These were established by affinity purification and mass spectrometry.

- Of these, one featured protein sharing between complexes (Gavin et al.[1]). In this study, they proposed a 'core-module-attachment' model. Core proteins are always present within a complex. Attachment proteins are single proteins that are sometimes but not always in a complex. Modules are groups of two or more strongly associated attachment proteins present in more than one complex.

- The aim of this study is to visualise the complexome as a network. This should provide a unique 'high-level' and biologically relevant view of the interactome.

The Complexome as a Network of Protein Complexes

- The dataset by Gavin et al[1] was used as a basis for this study.

- In our model, protein complexes are connected if they share one or more proteins [Fig. 1]. The lines between complexes represent the proteins in common.
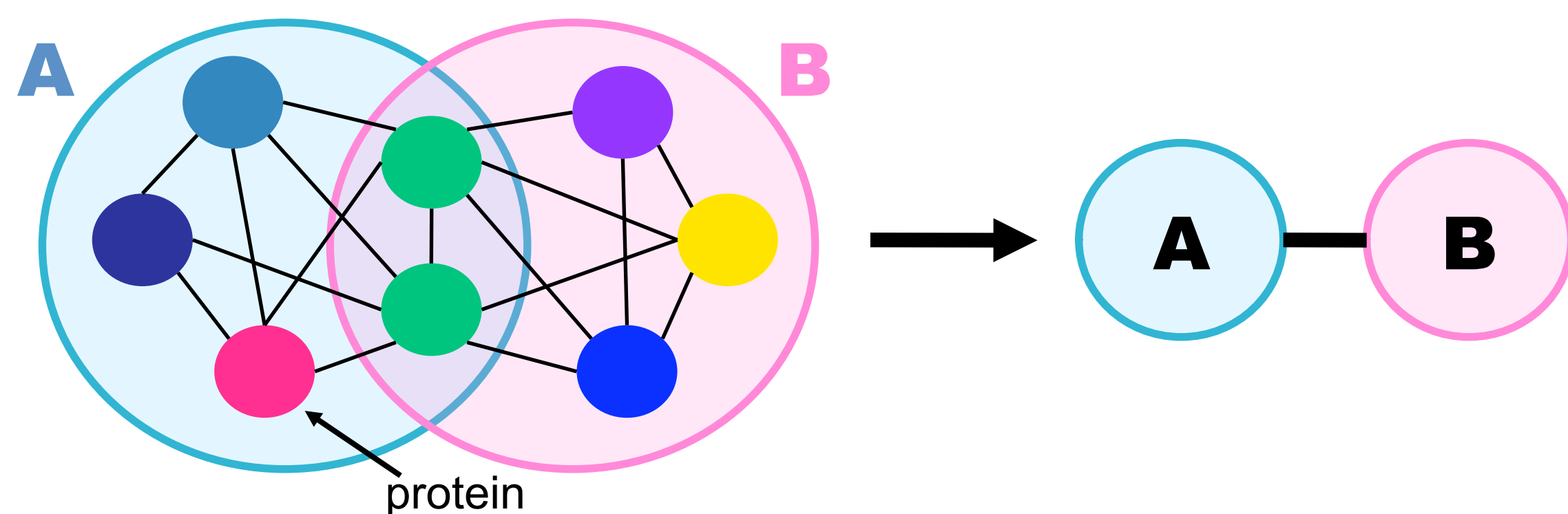

Figure 1: From interactome to complexome. In this example, two protein complexes A and B share 2 proteins. In the interactome, this is visualised as a highly interconnected cluster, and may be mistaken as a single complex. In the complexome, A and B are collapsed into single nodes, each representing a complex. The line drawn between them represents the 2 proteins they share.

- The GEOMI[2] platform was modified to visualise the complexome [Fig. 2]. This can be downloaded at **http://www.systemsbiology.org.au**.
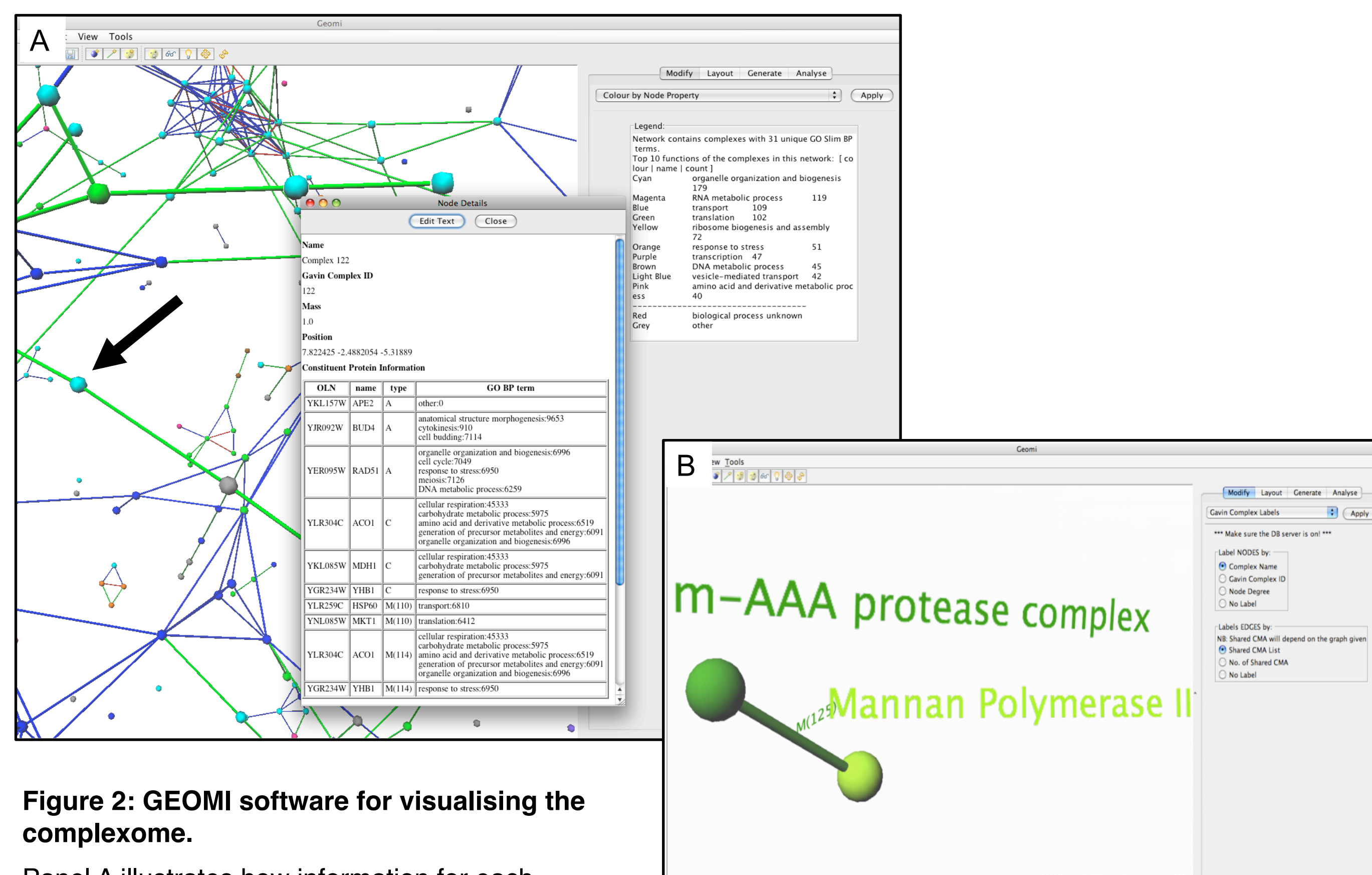

Figure 2: GEOMI software for visualising the complexome.

Panel A illustrates how information for each complex can be retrieved and displayed from an underlying relational database. In this case, complex 122 (arrow) has been selected via a right mouse button. The types of proteins in each complex (core, attachment, module) can be seen.

Panel B shows two complexes, joined together by module 125. The control panel (top right) has many options for labelling nodes and edges.

Structure and Topology of the Complexome Network

- The complexome network was constructed in two ways. Networks including links from shared core, module or attachment proteins were dense and uninterpretable [Fig. 3]. Networks whereby complexes were linked from shared core or module proteins showed some regions of high interconnectivity and other areas with no connections. This network is the CM (core-module) network.
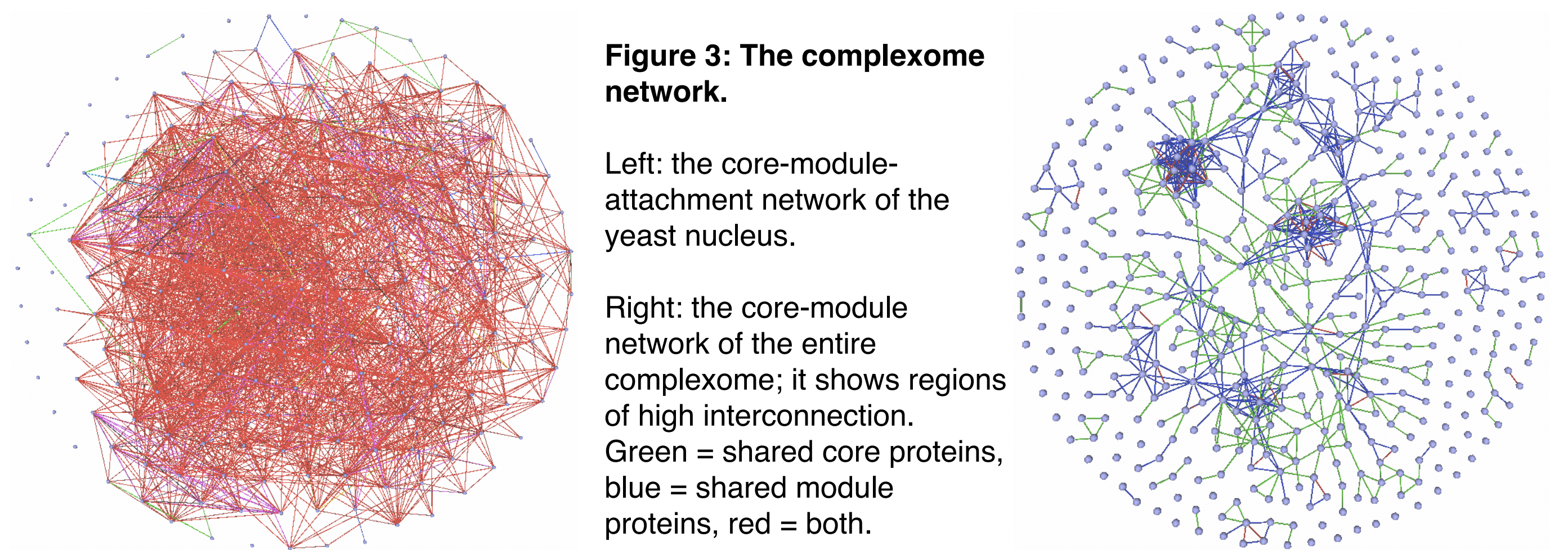

Figure 3: The complexome network.

Left: the core-module-attachment network of the yeast nucleus.

Right: the core-module network of the entire complexome; it shows regions of high interconnection. Green = shared core proteins, blue = shared module proteins, red = both.

- The CM network shows properties of scale-free networks. It has a degree exponent γ of 1.9, where scale-free networks have exponents of 2 to 3. It also has a clustering coefficient which is independent of node degree; a further scale-free property.

Functional Relationships of Interacting Complexes

- Gene ontology was used to investigate the functional relationships of interacting complexes.

- The biological processes of constituent proteins from each complex were tallied to assign a high-level function to each complex. This was then co-visualised with the CM network [Fig. 4].

- Many interacting complexes share common functions, suggesting the CM network is biologically relevant.

Figure 4: The complexome network, coloured by biological process. Node colour and line colours can be different, if shared proteins are of different process to those that are not.

Cyan – organelle organisation, Blue – RNA metabolic process, Orange – translation, Green – transport, Yellow – transcription, Pink – ribosome biogenesis, Black – other, Red – unknown. Singletons not shown.
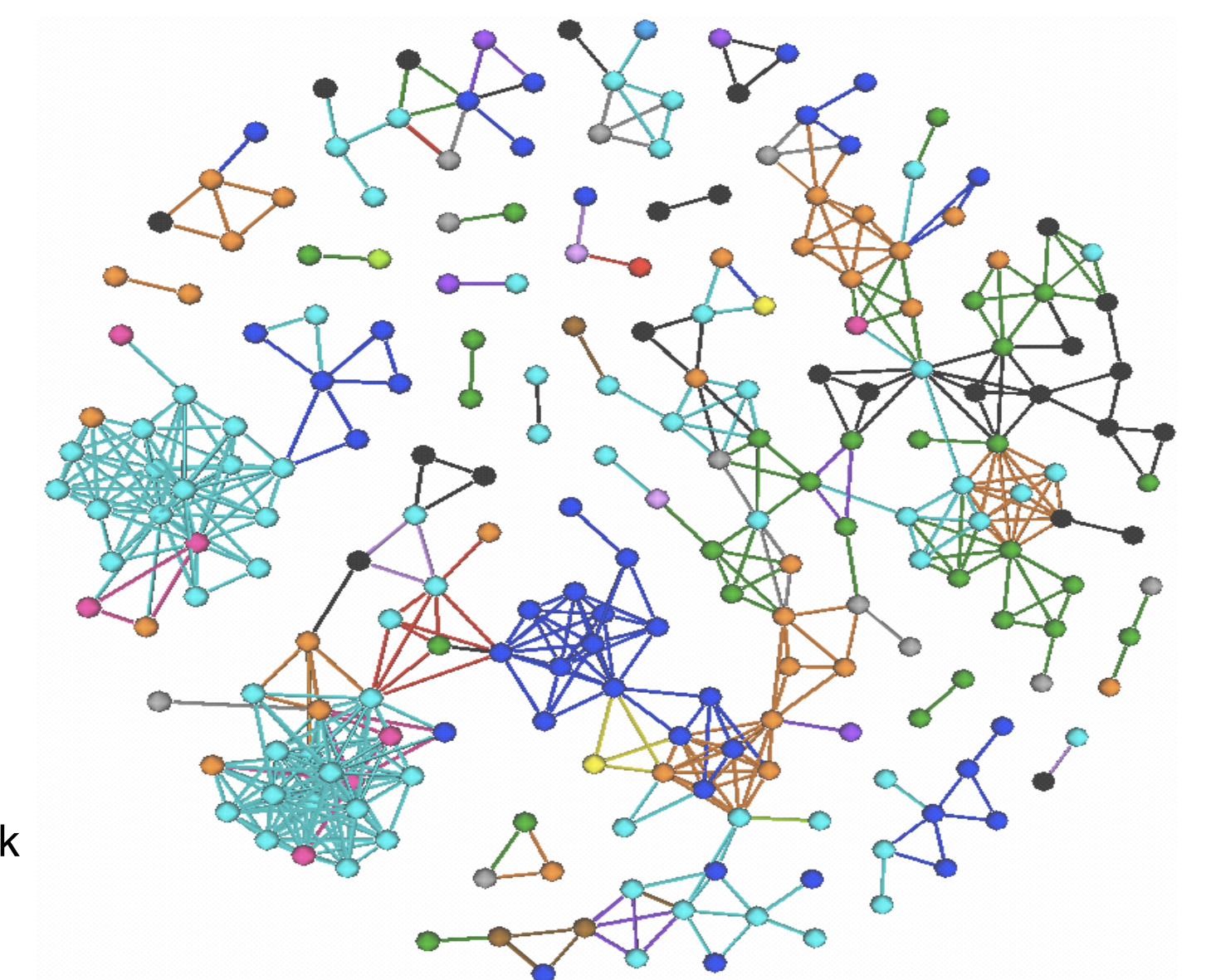
Interacting Complexes Reflect Higher Order of the Cell

- The higher order of the cell is reflected in interacting complexes [Fig. 5]. This suggests that 'guilt by association' will be useful to understand the function of novel complexes.

Figure 5: Detail of the complexome network. The RNA polymerase complexes I to III show interconnection, as do the SAGA, mediator and histone acetylases and deacetylases. Complexes 325 and 337 are likely to be involved in related processes.

Acknowledgements and References

[1]Gavin AC, et al. (2006). Proteome survey reveals modularity of the yeast cell machinery. *Nature*, **440**, 631-636.

[2]Ho E., Webber R. and Wilkins M. (2008). *Journal of Proteome Research*, **7**, 104-12.