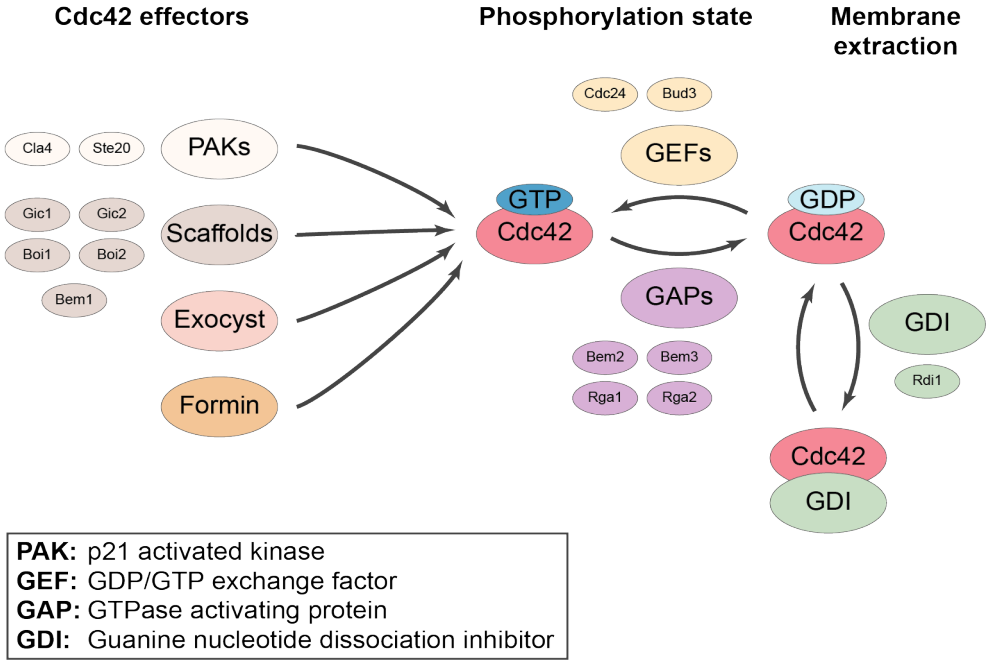
Investigating protein domains as the building blocks of the yeast polarity network

Saccharomyces cerevisiae proliferates through budding; a daughter cell grows by budding off on one side of the mother. The first step towards budding is the establishment of a Cdc42-based protein pattern on the cell membrane marking the site of bud-emergence. This pattern arises from local activation and accumulation of the GTPase Cdc42.

Cdc42 is highly regulated through several proteins that constitute the polarity protein network. Classically, each protein is categorised upon its effect on Cdc42 – there are, for example, scaffold proteins, GEFs (GDP/GTP exchange factors), GAPs (GTPase activating proteins) and a GDI (Guanine nucleotide dissociation inhibitor) (Fig.1). However, evolution experiments question the generality of this classification: In Saccharomyces cerevisiae cells the important polarity protein Bem1 was removed, resulting in a decreased fitness of the cells. The lineages were subsequently evolved for 1000 generations, and reached >90% of the fitness of their Bem1 ancestors at the end of the evolution. Sequencing their genomes showed that cells accomplished this by the removal of other polarity proteins (Bem3, Bem2, Nrp1) [1]. These experiments suggest that protein functions are distributed over the entire protein network, as the loss of one scaffold protein can be compensated with the loss of two GAPs and one other protein. Where does a proteins' functionality come from? Proteins are formally partitioned into protein domains – conserved parts with a given protein sequence and tertiary structure.

This project aims to investigate protein domains as the function-carrying building blocks proteins are made from, and to newly classify the yeast polarity proteins according to their domain-function relationship. Thereby new insights into the functionality distribution of this network might be gained. Bioinformatics approaches will be used, for example protein databases (Uniprot, Interpro) and protein sequence alignment tools such as HMMER.

Figure 2: The yeast polarity protein network. Figure based on [2].



[1] Laan et al. eLife 2015.
[2] Chiou et al. Ann. Rev. Cell Dev. Biol. 2017.

If you are interested in being part of this project, send an e-mail to s.tschirpke[at]tudelft.nl.