MODULAR COHERENCE OF PROTEIN DYNAMICS IN YEAST CELL POLARITY SYSTEM

酵母细胞极性系统中
蛋白动力学的模块一致性

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本篇论文实在一个系统的水平上研究酵母细胞两极中潜在的复杂的蛋白质相互作用及其动态关联

polar cortical domain (PCD)

这些蛋白质在PCD中局部化地执行形态发生的功能

构造PCD蛋白质的模块化的相互作用网络

在活体酵母细胞中测量PCD蛋白的动力学参数

基于模块化的网络结构建立蛋白质动力学模型

验证模型和模型的预测能力

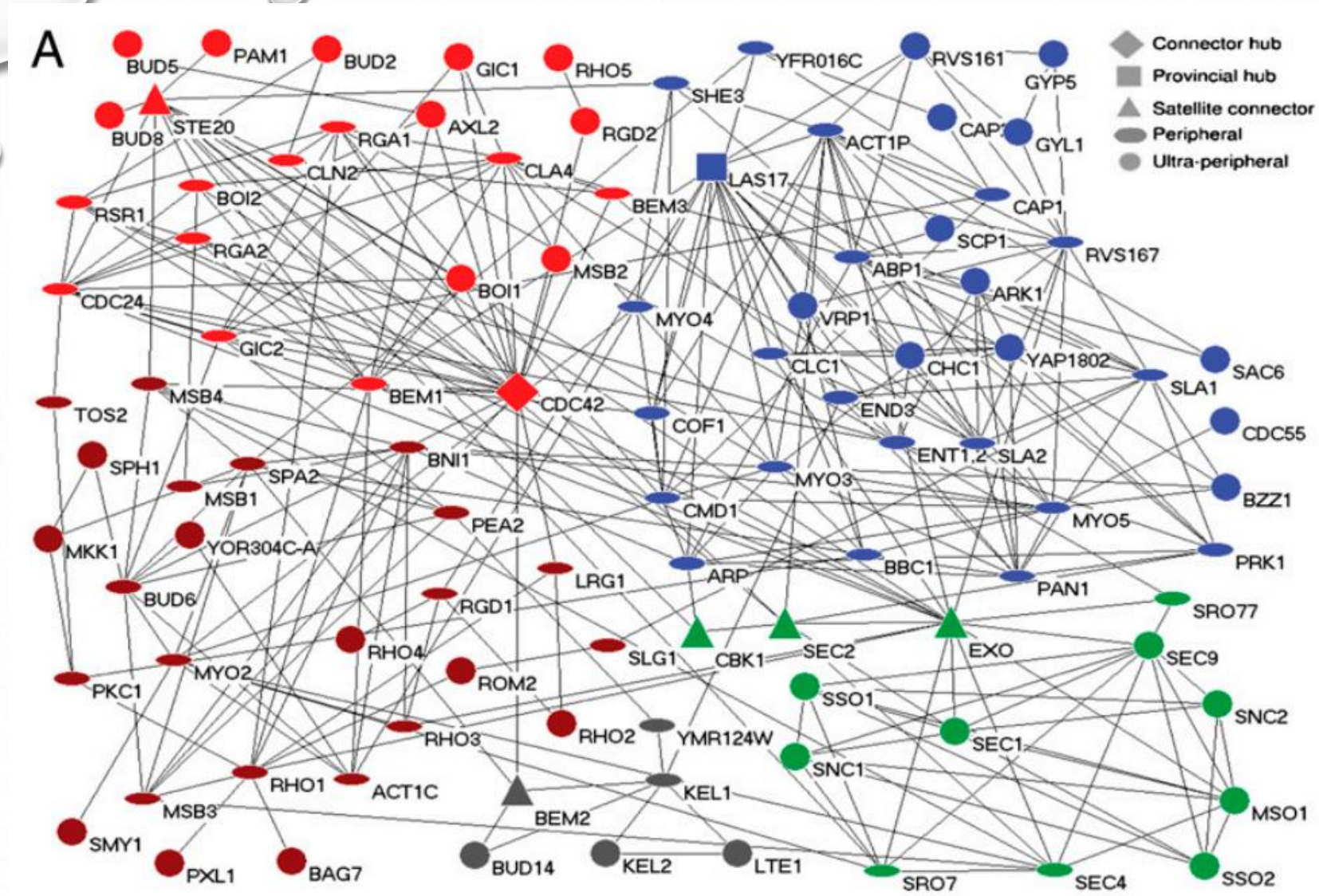
CONSTRUCTION OF A MODULAR NETWORK OF INTERACTIONS AMONG PCD PROTEINS

the genome-wide GFP-tagged yeast protein localization database

- 在酵母新生芽顶端的PCD蛋白质，加上Rho和Rab家族。
- 然后为了减少网络的复杂程度，将一些紧密相关的化合物作为网络中的单个节点

BioGrid database

- 包括99个节点和302个连接
- 有假阳性和缺失的链接
- 结合网络重构建和在模块识别中使模块最大化来控制错误敏感度的方案
- 得到了五个模块：Signaling, Transport, Endocytosis, Exocytosis, Mitotic Exit

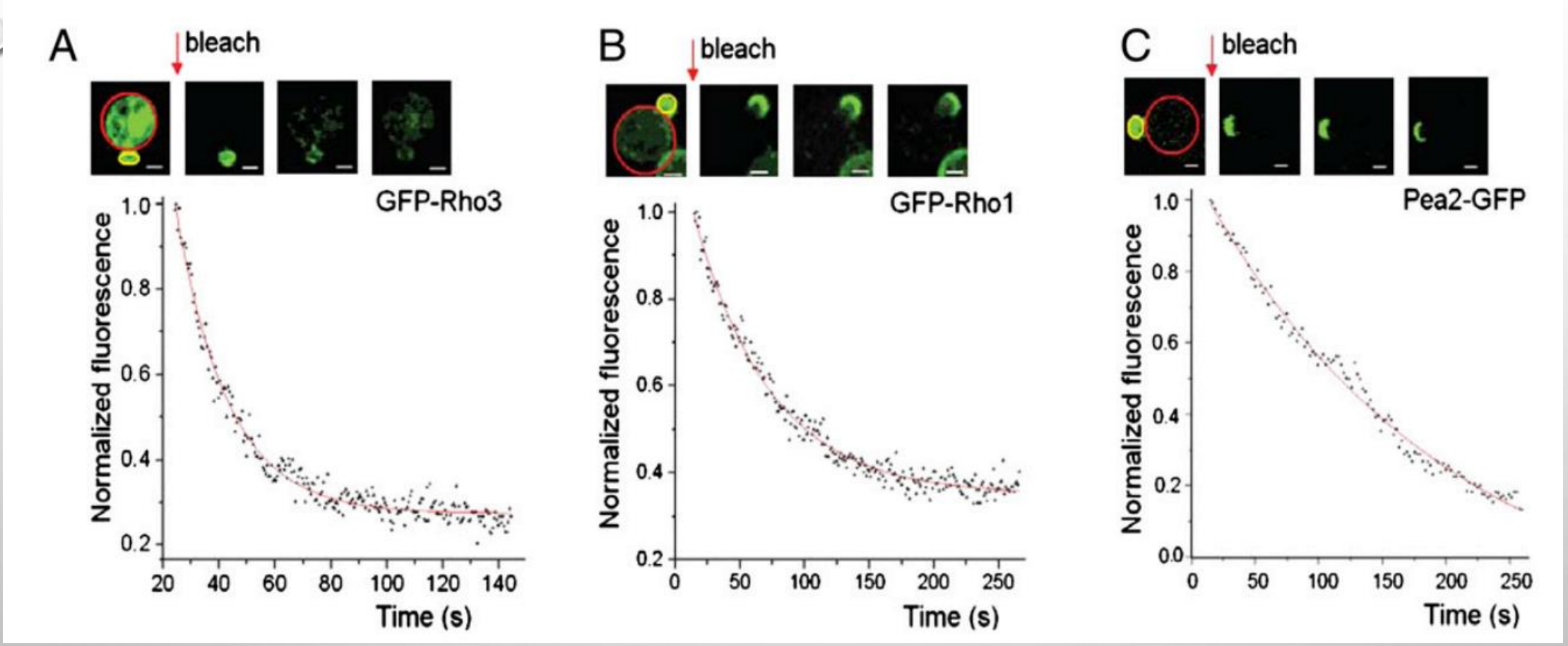


Signaling (red), Transport (brown), Endocytosis (blue), Exocytosis (green), Mitosis Exit regulation (gray)

MEASUREMENT OF PCD PROTEIN DYNAMICS IN LIVE YEAST CELLS

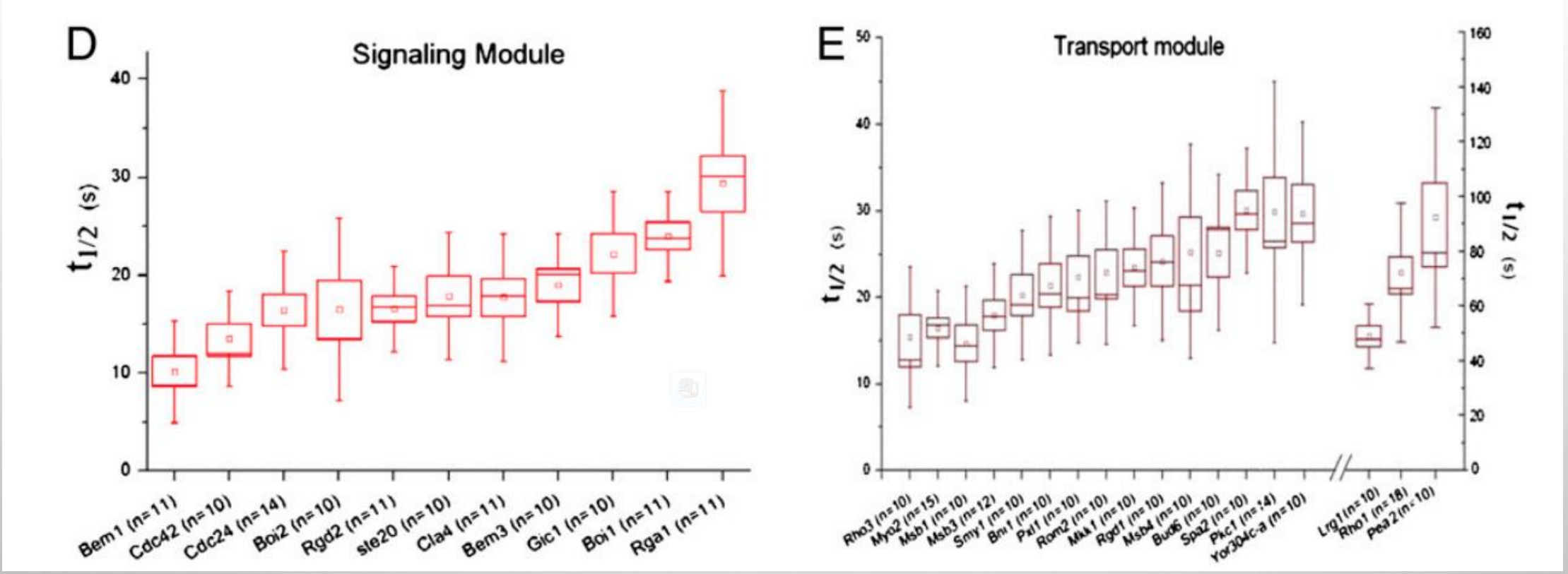
- Signaling(11)和Transport(18)模块
- 反义荧光漂白恢复技术（iFRAP）
- 荧光消失的半衰期（t1/2）近似蛋白质的residence time

MEASUREMENT OF PCD PROTEIN DYNAMICS IN LIVE YEAST CELLS



红圈：褪色区域；
黄圈：荧光测量区域
红箭头：褪色时间

MEASUREMENT OF PCD PROTEIN DYNAMICS IN LIVE YEAST CELLS



11个Signaling蛋白质

18个Transport蛋白质
前15个和后3个时间范围不同

MODELING PROTEIN DYNAMICS BASED ON A MODULAR NETWORK STRUCTURE

简化

- 为了简化模块网络，将给定的蛋白质P和其他蛋白质的相互作用简化为蛋白质P和模块的相互作用

N_p

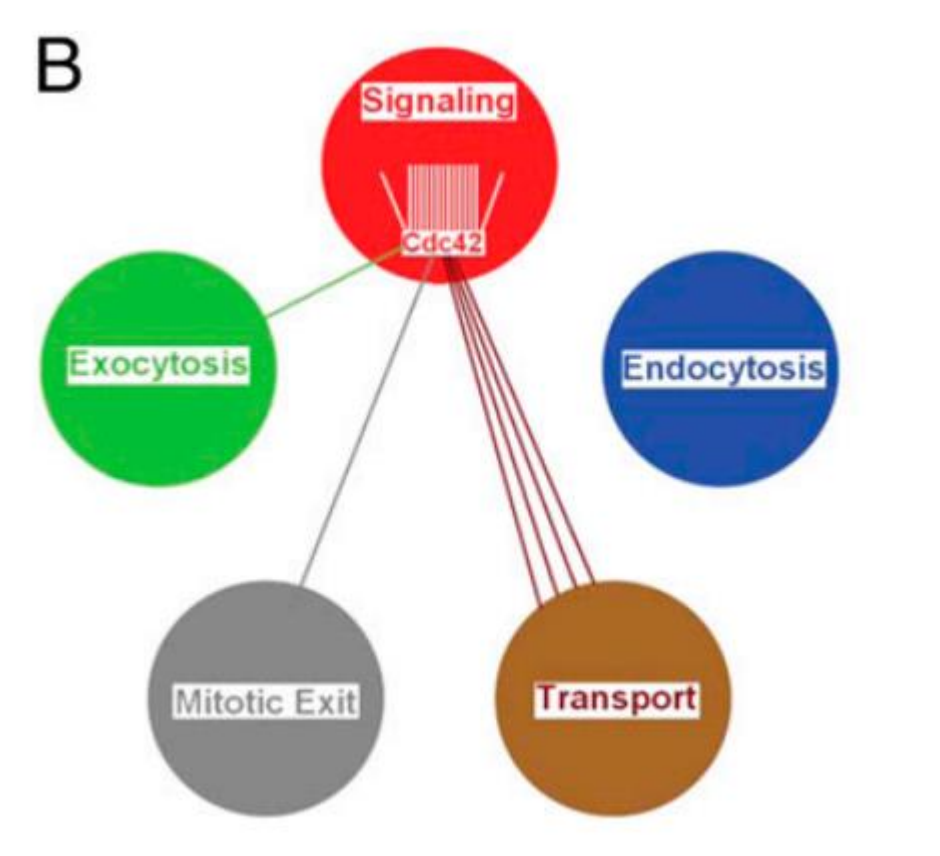
- 蛋白质P就可以描述成一个5维向量$N_p=\{N_{p,1},N_{p,2}N_{p,3}N_{p,4}N_{p,5}\}$
- $N_{p,i}$：和蛋白质P有相互作用的蛋白质中，属于第i个模块的蛋白质的数量

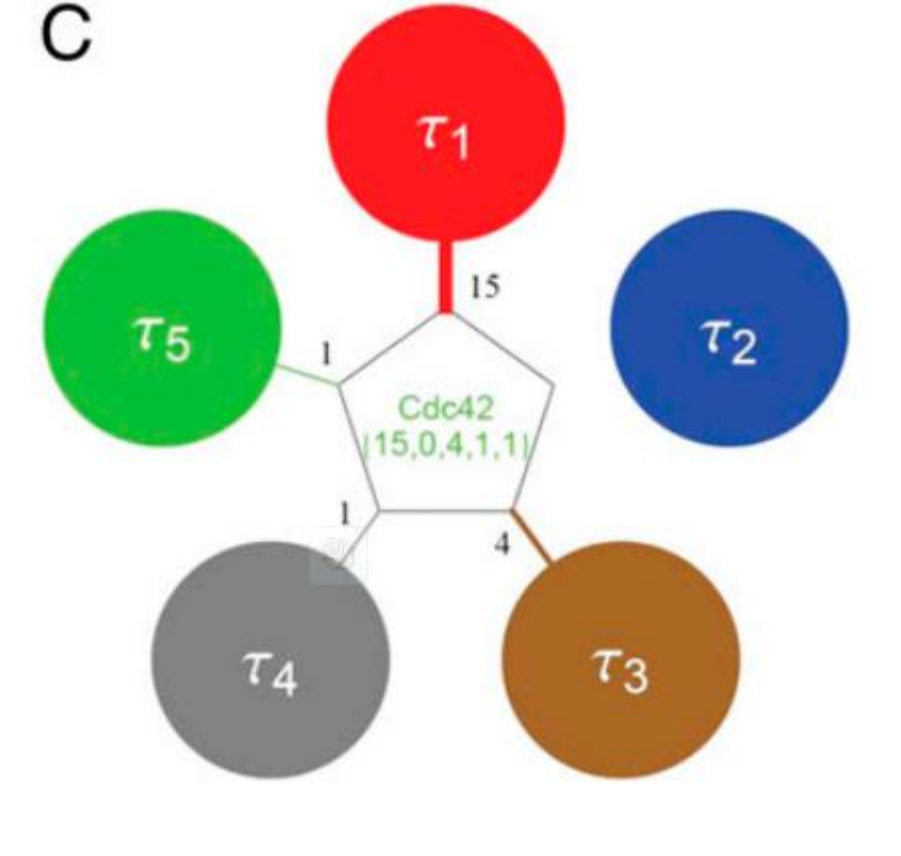
τ_i

- 用一个特征动力学参数 τ_i 代表模块i的特征
- τ_i有时间维度，但没有绝对的生物学意义

网络动态性

- 整个网络的动态特性就描述成另一个5维向量$\tau=\{\tau_1, \tau_2, \tau_3, \tau_4, \tau_5\}$





描述Cdc42和不同模块中的蛋白质的相互作用

N_{cdc42} = {15,0,4,1,1}

MODELING PROTEIN DYNAMICS BASED ON A MODULAR NETWORK STRUCTURE

$$N_p = \sum_{i=1}^{N} N_{p,i}$$

$$\tau_p = \sum_{i=1}^{N} \frac{N_{p,i}}{N_p} \tau_i$$

将τ_p作为蛋白质P的residence time

VALIDATION OF THE MODEL AND THE MODEL'S PREDICTIVE ABILITY

计算τ

- 选择10个蛋白质t1/2(τ_p)值作为训练集去计算模块的特征时间τ
- 所选蛋白质必须具备关于所有模块的信息量
- τ = {12.85, 27.27, 20.89, 82.20, 3.86} for the Signaling, Endocytosis, Transport, Mitotic Exit, and Exocytosis modules

预测t1/2

- 用计算出的τ预测其余19个蛋白质的t1/2(τ_p)

比较

- 计算出测量值(t1/2)和预测值(τ_p)得相关系数

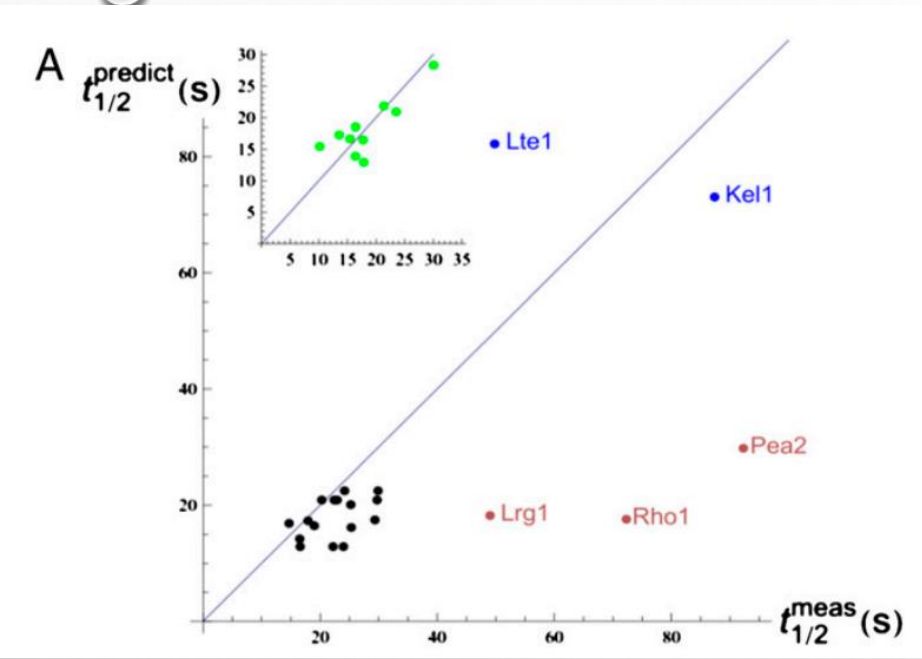
为了检验所取的10个蛋白质的训练集是否是最好的选择，随机挑选1000种10个蛋白质的组合方式进行测试。

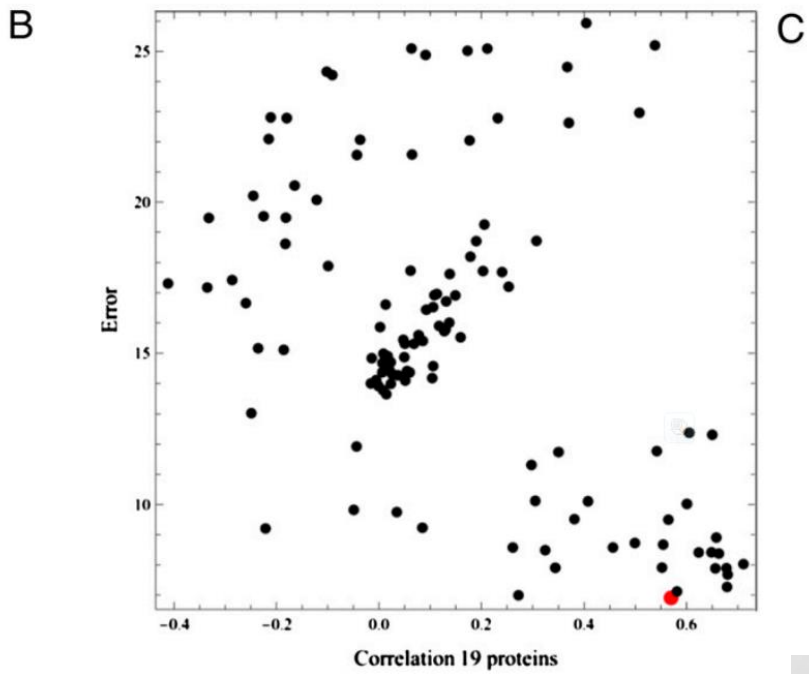
随机选择的蛋白质可能没有和所有的5个模块都有相互作用，或者是算出的τ是负的，舍弃这些结果。

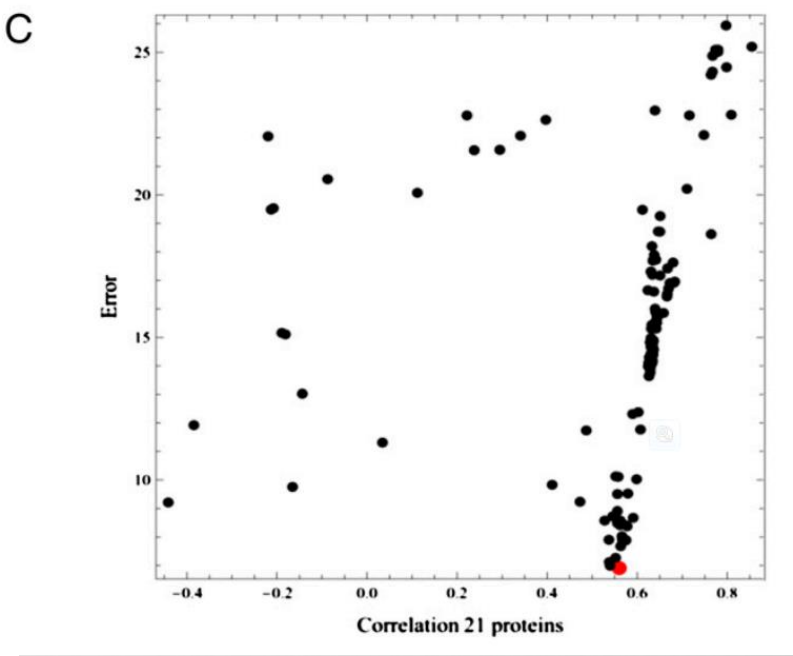
测试结果表明所选的10个蛋白质是最好的

VALIDATION OF THE MODEL AND THE MODEL'S PREDICTIVE ABILITY

Correlation of measured vs. model-predicted residence times and training set analysis.



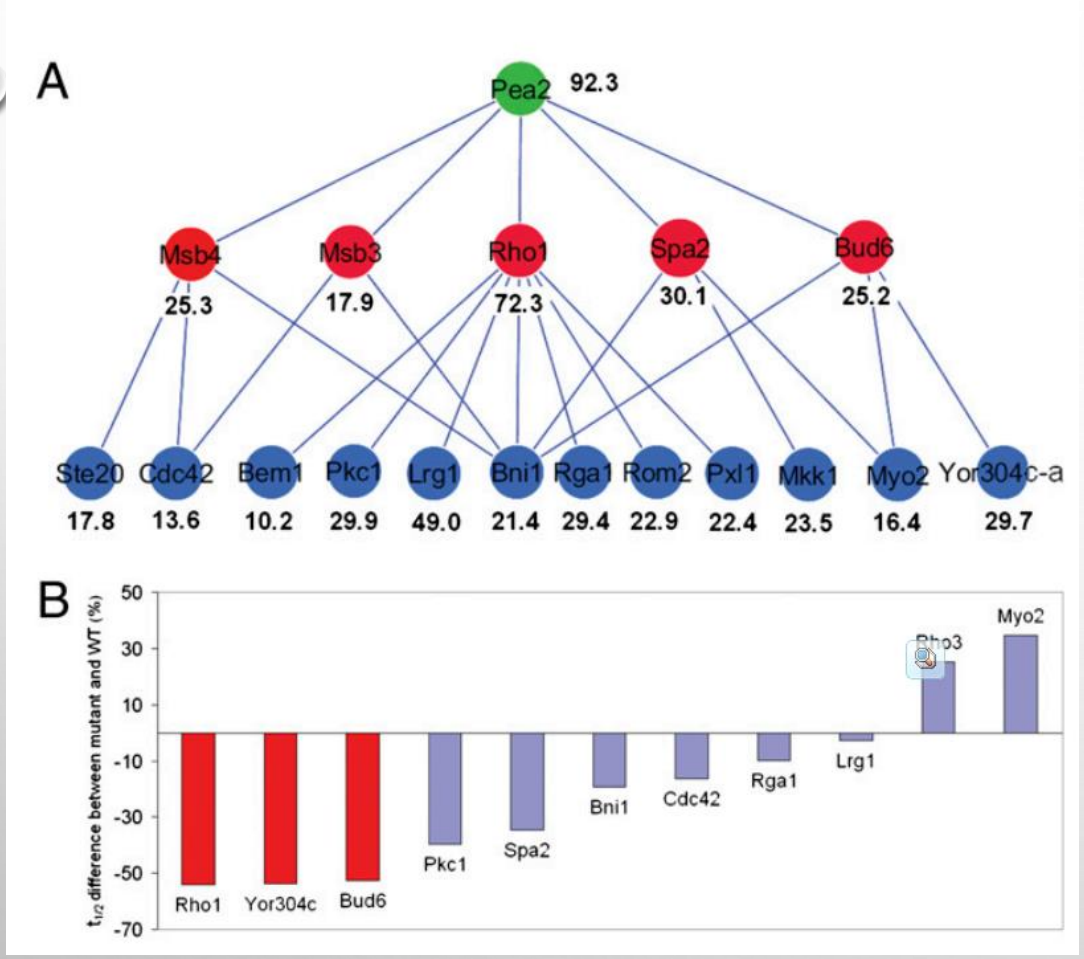




- the proteins in the Signaling and Transport modules (black dots)
- 2 proteins in the Mitotic Exit module (blue dots)
- (Pea2, Rho1, and Lrg1)异常值

- 红色是所选的训练集的结果
- Signaling和Transport模块的19种蛋白质

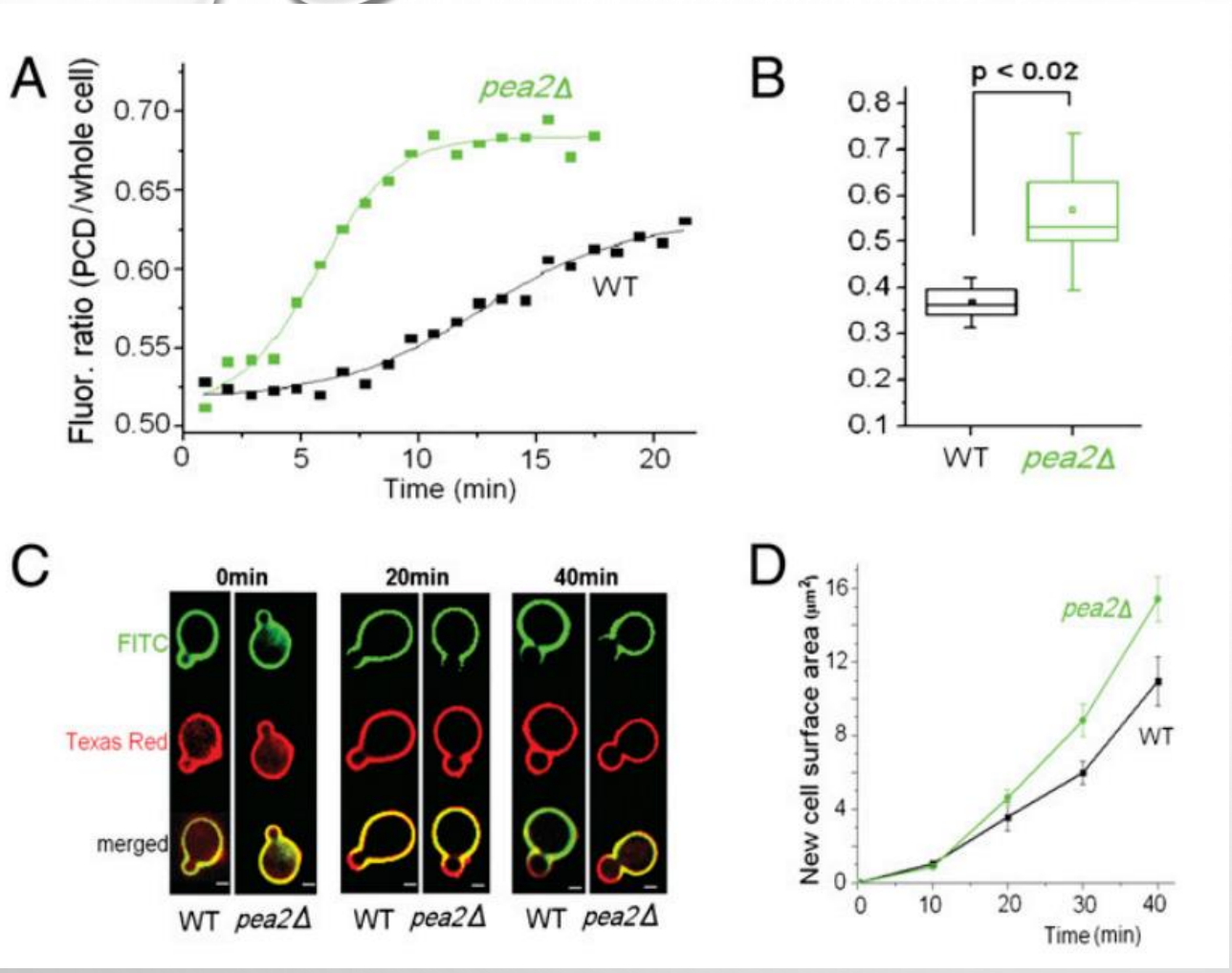
- Signaling和Transport的19种加上Mitotic Exit module的2种



Effects of the scaffold protein Pea2 on the dynamics of its interacting proteins.

(A) 红色的与**Pea2**作用更加紧密, 表示红色的比蓝色的有更长的**t1/2**值.

(B) **pea2**的突变型和野生型之间的不同。红色的和**Pea2**直接相互作用



对于建立和维护细胞极性来说，Pea2不是必须的

Effects of Pea2 on polarization kinetics and the rate of polarized growth.

(A) Observation of GFP-Rho1 polarization in WT (black) and pea2Δ cells (green) by time-lapse movies (Movies S4andS5). The plots show representative time-dependent changes in the average fluorescence intensity of GFP-Rho1 in the PCD, normalized against the average intensity in the whole cell.

(B) Quantification of the rates of Rho1 polarization in time-lapse movies as described in A. The polarization rate was defined as the slope at the inflection point of the sigmoid curve used for fitting. Statistical representation is the same as described in Fig. 2D.

(C) Example cell images for cell wall growth during budding in WT and pea2Δ cells by fluorescent Con A staining. Regions staining only with Texas Red Con A but not FITC Con A (red-only zones in merged images) represent a recent area of cell wall growth. (Scale bar: 2μm.)

(D) Quantification of cell wall growth during budding in WT and pea2Δ cells by fluorescent Con A staining. Plots show the increase in the area of growth over time. Averages of measurements from 15 to 25 cells per time point per strain are shown. Error bars reflect SEM

谢谢！