Synthetic Genetic Interaction in Yeast genes

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1 Introduction

Synthetic genetic interactions experiments are now being conduct to better understand cellular interactions. The generated data have already proven to be extremely valuable (**???**). Synthetic lethality especially defines a genetic interaction were the combination of mutations in two or more genes leads to cell death. The implications of synthetic lethal screens have been discussed in the context of drug development as synthetic lethal pairs could be used to selectively kill cancer cells, but leave normal cells relatively unharmed.

In this package, we propose statistical and computational tools for a systems biology approach in analyzing synthetic genetic interactions. Currently, our methods can be used to find relationships between synthetic genetic interactions and cellular organizational units such multi-protein complexes or sequence motifs.

2 Synthetic genetic interaction data

Several synthetic genetic datasets are now publicly available. In this package we currently propose 6 datasets:

- **?** Systematic genetic analysis with ordered arrays of yeast deletion
- **?** DNA integrity experiment in *S. cerevisiae*
- **?** Systematic yeast synthetic lethal and synthetic dosage lethal screens identify genes required for chromosome segregation.
- **?** Genetic Interaction Data (EMAP) from the yeast early secretory pathway
- **?** Functional dissection of protein complexes involved in yeast chromosome biology using a genetic interaction map.
- **?** Synthetic genetic interaction data from as recorded by the Saccharomyces Genome database in January, 2007.

In this package and as reported by most authors, we use the terms *query genes* for the genes that are specifically tested by the experimenter and *array genes* for the target genes usually spotted on a array (*e.g.,* SGA, dSLAM). We note however that an analogy can be made with the concept of *bait* and *prey* terms used in proteomic experiments (*e.g.,* Y2H, APMS).

2.1 Synthetic genetic array data, Tong et al. (2004)

? used the *Synthetic Genetic Array technology* or SGA to investigate synthetic genetic interaction in *S. cerevisiae*. The package SLGI contains both the raw and preprocessed data from **?**. To access those data you first need to load the package SLGI and the yeast genome annotation package (org.Sc.sgd.db):

```
> library("SLGI")
> library("org.Sc.sgd.db")
> ##loading Tong et al data
> data(SGA)
> data(Atong)
```

Data `SGA` contains the systematic names of all the 4655 genes tested by **?**, including both the ones that were reported as presenting synthetic genetic interactions and the ones that were not (`SGAraw` corresponds to the original list parsed from table1 of **?** supplementary material).

We can verify that the genes reported by **?** are well characterized. To that aim, we use the yeast annotation data package org.Sc.sgd.db:

```
> rejected <- length(intersect(SGA, org.Sc.sgdREJECTORF))
```

We note that at this time 0 genes (out of the 4655) are among the rejected ORF listed by the *Saccharomyces* Genome Database (SGD http://www.yeastgenome.org/). If one want to update common gene names or alias to systematic names, one can use the following:

```
> updateSGA=mget(SGA, org.Sc.sgdCOMMON2ORF, ifnotfound = NA )
```

The `tong2004raw` data.frame contains the original data reported by **?** as Table S1 in their online supporting material. The `Atong` data contains the association matrix extracted from the `tong2004raw` data.frame. The gene names were updated for systematic gene names. They selected 132 query genes that are known involved in a chosen set of molecular functions.

There are 11 essential genes found in the query genes. **?** pointed out that some of the query genes are partially functioning alleles of essential genes. So, we assumed these genes are fine. There are also 3 essential genes in the reported array genes that showed synthetic lethal (SL) interaction with at least one of the query genes. We checked these three genes. Two of them, "YJL174W" and "YPL075W" , are annotated both "lethal" and "viable" in the `SGD` database. The other gene, "YBR121C", is "lethal". We don't have the resources to tract down why this gene appears on the `SGA` array **?**.

2.1.1 Synthetic lethal and synthetic dosage lethal screens, Measday et al (2005)

? perform some systematic yeast synthetic lethal and synthetic dosage lethal screens using the SGA approach (**?**). They first tested 14 query genes and found 84 non-essential genes that synthetically interact with at least one query gene (`SLchr`). Then they tested interaction between 3 query genes and the genome wide set of deletion strains under 3 different temperatures. They found 141 array genes that interact at least with one query gene (`SDL`). They identified genes required for chromosome segregation.

2.2 DNA integrity experiment in S. cerevisiae, Pan et al (2006)

The package contains raw and preprocessed data from **?** obtained in Boeke's lab.

```
> data(Boeke2006raw)
> data(Boeke2006)
```

`Boeke2006raw` is a data frame with 5775 observations and `Boeke2006` is an incidence matrix reporting the systematic genetic interactions identified between 74 query genes and the deletion gene set in **?** (see man pages for more details).

The technology used by Boeke and collaborators is slightly different from the approach taken by **?**. The used heterozygote diploid-based synthetic lethality analyzed by microarray (dSLAM). The 21991 probes spotted on the dSLAM array are available by calling `dSLAM.GPL1444` or `dSLAM` (see man pages for more details).

2.3 Genetic Interaction Data (EMAP), Schuldiner et al (2005) and Collins (2007)

We also collected data generated by Collins and collaborators. These data are different from the other as they have be heavily preprocessed using their own procedure, EMAP or epistatic miniarray profiles. Those data are presented as incidence matrix and are accompanied by some metadata, e.g., systematic names and mutated allele.

```
> ## Schuldiner et al. (2005)
> data(gi2005)
> data(gi2005.metadata)
```

2.4 Saccharomyces Genome database

We provide synthetic genetic interaction data as recorded by the Saccharomyces Genome database in January, 2007. Data can be accessed using `SGD.SL`, synthetic lethal, `SGD.SynRescue`, synthetic rescue, and `SGD.SynGrowthDefect`, synthetic growth defect.

3 Transcription Factor data

The transcription factor binding affinities data were extracted from **?**. They represented as an matrix where rows are *S. cerevisiae* systematic gene names and columns known transcription factor. The value in each entry represents the p-value, as reported by **?**, for the transcription factor (TF) binding upstream of the gene.

```
> data(TFmat)
```

4 Example of analysis: Synthetic genetic interactions and multi-protein complexes

To integrate synthetic genetic interactions with multi-protein complexes, we can make use of the interactome as defined in the ScISI package. The ScISI package or *In Silico Interactome for Saccharomyces cerevisiae* provides an interactome built for computational experimentation. The `ScISI` is binary incidence matrix where the rows are indexed by the gene locus names and the columns are indexed by the identification codes for the protein complexes based on the repository from where they are obtained. This interactome is currently built from the Intact, Gene Ontology and Mips curated databases, and estimated protein complexes from the apComplex package. In this vignette, we will make use of a subset of the `ScISI` interactome, the `ScISIC` data, that only contains the data from the curated databases.

```
> library(ScISI)
> data(ScISIC)
> ScISIC[1:5, 1:5]
```

```
            EBI-913756 EBI-876785 EBI-852570 EBI-866976 EBI-1180400
EBI-913756           0          0          0          0           0
EBI-876785           0          0          0          0           0
EBI-852570           0          0          0          0           0
EBI-866976           0          0          0          0           0
EBI-1180400          0          0          0          0           0
```

As an example we will use the data generated by **?**.First, one need to reduce the interactome matrix and genetic interaction matrix to the same list of genes. This can be done using the `gi2Interactome` function.

```
> data(Boeke2006)
> data(dSLAM)
> dim(Boeke2006)
```

```
[1]  74 843
```

```
> Boeke2006red <- gi2Interactome(Boeke2006, ScISIC)
> dim(Boeke2006red)

[1]  46 320
```

Next we can identify multi-protein complexes that present synthetic interaction among their proteins (**within interaction) or share synthetic interaction with other multi-protein complex (between interaction) using the** `getInteraction` **function. This function requires the incidence matrix, the array list and the interactome of interest.**

```
> interact <- getInteraction(Boeke2006red, dSLAM, ScISIC)
```

Then, one might want to know how what are the multi-protein complexes that share at least n interactions:

```
> intSummary <- iSummary(interact$bwMat, n=5)

---------Count:  7 -----------
GO:0031390  Ctf18 RFC-like complex
EBI-1252538  Ctf18 RFC-like complex
---------Count: 12 -----------
GO:0000417  HIR complex
EBI-1236334  HIR complex
---------Count:  9 -----------
GO:0030870  Mre11 complex
EBI-1236334  Mre11 complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
EBI-1236334  Ctf18 RFC-like complex
---------Count:  6 -----------
GO:0031390  Ctf18 RFC-like complex
EBI-1251060  Ctf18 RFC-like complex
---------Count:  9 -----------
GO:0000502  proteasome complex
GO:0000118  histone deacetylase complex
---------Count:  6 -----------
GO:0030015  CCR4-NOT core complex
GO:0000118  histone deacetylase complex
---------Count:  8 -----------
GO:0031415  NatA complex
GO:0000118  histone deacetylase complex
---------Count:  9 -----------
GO:0043529  GET complex
```

```
GO:0000118  histone deacetylase complex
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
GO:0000118  histone deacetylase complex
---------Count:  8 -----------
MIPS-370  Protein N-acetyltransferase
GO:0000118  histone deacetylase complex
---------Count:  6 -----------
MIPS-360  Proteasome
GO:0000118  histone deacetylase complex
---------Count:  7 -----------
GO:0000502  proteasome complex
GO:0000119 Not found (possibly deprecated)
---------Count: 10 -----------
GO:0043529  GET complex
GO:0000119 Not found (possibly deprecated)
---------Count:  6 -----------
GO:0005694  chromosome
GO:0000119 Not found (possibly deprecated)
---------Count:  6 -----------
GO:0000812  Swr1 complex
GO:0000151  ubiquitin ligase complex
---------Count:  6 -----------
GO:0030870  Mre11 complex
GO:0000151  ubiquitin ligase complex
---------Count:  6 -----------
GO:0035267  NuA4 histone acetyltransferase complex
GO:0000151  ubiquitin ligase complex
---------Count:  7 -----------
GO:0005694  chromosome
GO:0000151  ubiquitin ligase complex
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
GO:0000151  ubiquitin ligase complex
---------Count:  8 -----------
GO:0030529  intracellular ribonucleoprotein complex
GO:0000417  HIR complex
---------Count:  6 -----------
GO:0032806  carboxy-terminal domain protein kinase complex
GO:0000417  HIR complex
---------Count:  9 -----------
GO:0000508 Not found (possibly deprecated)
```

```
GO:0000502  proteasome complex
---------Count:  6 -----------
GO:0016469  proton-transporting two-sector ATPase complex
GO:0000502  proteasome complex
---------Count: 15 -----------
GO:0030529  intracellular ribonucleoprotein complex
GO:0000502  proteasome complex
---------Count:  6 -----------
GO:0030870  Mre11 complex
GO:0000502  proteasome complex
---------Count:  6 -----------
GO:0030897  HOPS complex
GO:0000502  proteasome complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0000502  proteasome complex
---------Count:  7 -----------
GO:0033263  CORVET complex
GO:0000502  proteasome complex
---------Count: 11 -----------
GO:0005694  chromosome
GO:0000502  proteasome complex
---------Count: 15 -----------
GO:0005840  ribosome
GO:0000502  proteasome complex
---------Count:  6 -----------
MIPS-240.20  HDB complex
GO:0000502  proteasome complex
---------Count:  6 -----------
MIPS-260.80  Class C Vps protein complex
GO:0000502  proteasome complex
---------Count:  6 -----------
MIPS-220  H+-transporting ATPase, vacuolar
GO:0000502  proteasome complex
---------Count:  6 -----------
GO:0030015  CCR4-NOT core complex
GO:0000508 Not found (possibly deprecated)
---------Count:  9 -----------
GO:0031415  NatA complex
GO:0000508 Not found (possibly deprecated)
---------Count: 14 -----------
GO:0043529  GET complex
```

```
GO:0000508 Not found (possibly deprecated)
---------Count:  7 -----------
GO:0005694  chromosome
GO:0000508 Not found (possibly deprecated)
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
GO:0000508 Not found (possibly deprecated)
---------Count:  9 -----------
MIPS-370  Protein N-acetyltransferase
GO:0000508 Not found (possibly deprecated)
---------Count:  8 -----------
GO:0030015  CCR4-NOT core complex
GO:0000812  Swr1 complex
---------Count:  8 -----------
GO:0031415  NatA complex
GO:0000812  Swr1 complex
---------Count:  6 -----------
GO:0043529  GET complex
GO:0000812  Swr1 complex
---------Count:  6 -----------
GO:0005694  chromosome
GO:0000812  Swr1 complex
---------Count:  8 -----------
MIPS-510.190.110  CCR4 complex
GO:0000812  Swr1 complex
---------Count:  8 -----------
MIPS-370  Protein N-acetyltransferase
GO:0000812  Swr1 complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0000814  ESCRT II complex
---------Count:  6 -----------
GO:0031415  NatA complex
GO:0000814  ESCRT II complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
GO:0000814  ESCRT II complex
---------Count:  6 -----------
MIPS-360  Proteasome
GO:0000814  ESCRT II complex
---------Count:  6 -----------
GO:0030015  CCR4-NOT core complex
```

```
GO:0000815  ESCRT III complex
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
GO:0000815  ESCRT III complex
---------Count:  6 -----------
GO:0043529  GET complex
GO:0000938  GARP complex
---------Count:  8 -----------
GO:0043529  GET complex
GO:0005667  transcription factor complex
---------Count:  6 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0005678 Not found (possibly deprecated)
---------Count:  6 -----------
GO:0033263  CORVET complex
GO:0005678 Not found (possibly deprecated)
---------Count:  8 -----------
GO:0005694  chromosome
GO:0005678 Not found (possibly deprecated)
---------Count:  7 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0005680  anaphase-promoting complex
---------Count:  6 -----------
GO:0030870  Mre11 complex
GO:0005732  small nucleolar ribonucleoprotein complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0005871  kinesin complex
---------Count:  6 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0005875  microtubule associated complex
---------Count:  6 -----------
GO:0043529  GET complex
GO:0008023  transcription elongation factor complex
---------Count:  7 -----------
GO:0005694  chromosome
GO:0008540  proteasome regulatory particle, base subcomplex
---------Count: 16 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0016272  prefoldin complex
---------Count:  9 -----------
GO:0031415  NatA complex
```

```
GO:0016272  prefoldin complex
---------Count:  6 ----------
GO:0005838  proteasome regulatory particle
GO:0016272  prefoldin complex
---------Count:  9 ----------
MIPS-370  Protein N-acetyltransferase
GO:0016272  prefoldin complex
---------Count:  6 ----------
MIPS-360  Proteasome
GO:0016272  prefoldin complex
---------Count: 10 ----------
GO:0030015  CCR4-NOT core complex
GO:0016469  proton-transporting two-sector ATPase complex
---------Count:  6 ----------
GO:0031415  NatA complex
GO:0016469  proton-transporting two-sector ATPase complex
---------Count: 16 ----------
GO:0043529  GET complex
GO:0016469  proton-transporting two-sector ATPase complex
---------Count: 10 ----------
MIPS-510.190.110  CCR4 complex
GO:0016469  proton-transporting two-sector ATPase complex
---------Count:  6 ----------
MIPS-370  Protein N-acetyltransferase
GO:0016469  proton-transporting two-sector ATPase complex
---------Count:  6 ----------
GO:0031415  NatA complex
GO:0016514  SWI/SNF complex
---------Count:  6 ----------
MIPS-370  Protein N-acetyltransferase
GO:0016514  SWI/SNF complex
---------Count:  8 ----------
GO:0031415  NatA complex
GO:0016585 Not found (possibly deprecated)
---------Count:  8 ----------
MIPS-370  Protein N-acetyltransferase
GO:0016585 Not found (possibly deprecated)
---------Count: 10 ----------
GO:0043529  GET complex
GO:0017119  Golgi transport complex
---------Count: 11 ----------
GO:0030529  intracellular ribonucleoprotein complex
```

```
GO:0030015  CCR4-NOT core complex
---------Count:  6 -----------
GO:0030870  Mre11 complex
GO:0030015  CCR4-NOT core complex
---------Count:  6 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0030015  CCR4-NOT core complex
---------Count:  6 -----------
GO:0000274  mitochondrial proton-transporting ATP synthase, stator stalk
GO:0030015  CCR4-NOT core complex
---------Count:  6 -----------
MIPS-240.20  HDB complex
GO:0030015  CCR4-NOT core complex
---------Count:  9 -----------
MIPS-420.50  F0/F1 ATP synthase (complex V)
GO:0030015  CCR4-NOT core complex
---------Count: 12 -----------
GO:0030870  Mre11 complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 18 -----------
GO:0031415  NatA complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count:  9 -----------
GO:0033062  Rhp55-Rhp57 complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count:  8 -----------
GO:0033551  monopolin complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 11 -----------
GO:0043529  GET complex
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 13 -----------
GO:0005694  chromosome
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 12 -----------
GO:0005838  proteasome regulatory particle
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 11 -----------
MIPS-510.190.110  CCR4 complex
```

```
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 18 -----------
MIPS-370  Protein N-acetyltransferase
GO:0030529  intracellular ribonucleoprotein complex
---------Count: 12 -----------
MIPS-360  Proteasome
GO:0030529  intracellular ribonucleoprotein complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
GO:0031415  NatA complex
GO:0030870  Mre11 complex
---------Count:  9 -----------
GO:0032806  carboxy-terminal domain protein kinase complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
GO:0033551  monopolin complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
GO:0043234  protein complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
GO:0043529  GET complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
GO:0046540  U4/U6 x U5 tri-snRNP complex
GO:0030870  Mre11 complex
---------Count: 10 -----------
GO:0005694  chromosome
GO:0030870  Mre11 complex
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
GO:0030870  Mre11 complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
GO:0030870  Mre11 complex
---------Count:  9 -----------
MIPS-360  Proteasome
GO:0030870  Mre11 complex
---------Count:  9 -----------
GO:0031390  Ctf18 RFC-like complex
```

```
GO:0030897  HOPS complex
---------Count:  6 ----------
GO:0031415  NatA complex
GO:0030897  HOPS complex
---------Count:  8 ----------
GO:0043529  GET complex
GO:0030897  HOPS complex
---------Count:  6 ----------
MIPS-370  Protein N-acetyltransferase
GO:0030897  HOPS complex
---------Count:  6 ----------
GO:0031415  NatA complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0032806  carboxy-terminal domain protein kinase complex
GO:0031390  Ctf18 RFC-like complex
---------Count: 12 ----------
GO:0033263  CORVET complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0033551  monopolin complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  9 ----------
GO:0033597  mitotic checkpoint complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0035267  NuA4 histone acetyltransferase complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0043529  GET complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0046695  SLIK (SAGA-like) complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
GO:0000786  nucleosome
GO:0031390  Ctf18 RFC-like complex
---------Count: 13 ----------
GO:0005694  chromosome
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 ----------
MIPS-125.10.10  Ddc1p-Mec3p complex
```

```
GO:0031390  Ctf18 RFC-like complex
---------Count:  9 -----------
MIPS-260.80  Class C Vps protein complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 -----------
MIPS-310  Nuclear pore complex (NPC)
GO:0031390  Ctf18 RFC-like complex
---------Count:  9 -----------
MIPS-510.190.110  CCR4 complex
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
GO:0031390  Ctf18 RFC-like complex
---------Count:  6 -----------
MIPS-360  Proteasome
GO:0031390  Ctf18 RFC-like complex
---------Count:  8 -----------
GO:0033263  CORVET complex
GO:0031415  NatA complex
---------Count:  6 -----------
GO:0046540  U4/U6 x U5 tri-snRNP complex
GO:0031415  NatA complex
---------Count: 12 -----------
GO:0005681  spliceosomal complex
GO:0031415  NatA complex
---------Count: 13 -----------
GO:0005694  chromosome
GO:0031415  NatA complex
---------Count:  6 -----------
GO:0005840  ribosome
GO:0031415  NatA complex
---------Count:  6 -----------
MIPS-240.20  HDB complex
GO:0031415  NatA complex
---------Count:  6 -----------
MIPS-260.80  Class C Vps protein complex
GO:0031415  NatA complex
---------Count:  6 -----------
MIPS-510.190.50  SWI/SNF transcription activator complex
GO:0031415  NatA complex
---------Count:  6 -----------
MIPS-220  H+-transporting ATPase, vacuolar
```

```
GO:0031415  NatA complex
---------Count:  6 -----------
GO:0033551  monopolin complex
GO:0032806  carboxy-terminal domain protein kinase complex
---------Count:  6 -----------
GO:0043529  GET complex
GO:0032806  carboxy-terminal domain protein kinase complex
---------Count:  7 -----------
GO:0005694  chromosome
GO:0032806  carboxy-terminal domain protein kinase complex
---------Count:  8 -----------
GO:0043529  GET complex
GO:0033263  CORVET complex
---------Count:  8 -----------
MIPS-370  Protein N-acetyltransferase
GO:0033263  CORVET complex
---------Count:  7 -----------
MIPS-360  Proteasome
GO:0033263  CORVET complex
---------Count:  6 -----------
GO:0005694  chromosome
GO:0033551  monopolin complex
---------Count: 10 -----------
GO:0043529  GET complex
GO:0033588  Elongator holoenzyme complex
---------Count:  6 -----------
GO:0005694  chromosome
GO:0035267  NuA4 histone acetyltransferase complex
---------Count:  8 -----------
GO:0005694  chromosome
GO:0043234  protein complex
---------Count:  8 -----------
GO:0048188  Set1C/COMPASS complex
GO:0043529  GET complex
---------Count:  6 -----------
GO:0000220  vacuolar proton-transporting V-type ATPase, V0 domain
GO:0043529  GET complex
---------Count: 10 -----------
GO:0000221  vacuolar proton-transporting V-type ATPase, V1 domain
GO:0043529  GET complex
---------Count: 22 -----------
GO:0005694  chromosome
```

```
GO:0043529  GET complex
---------Count:  6 ----------
GO:0005840  ribosome
GO:0043529  GET complex
---------Count:  6 ----------
MIPS-133.40  Srb10p complex
GO:0043529  GET complex
---------Count:  6 ----------
MIPS-240.20  HDB complex
GO:0043529  GET complex
---------Count: 10 ----------
MIPS-260.20  Clathrin-associated protein (AP) complex
GO:0043529  GET complex
---------Count:  8 ----------
MIPS-260.80  Class C Vps protein complex
GO:0043529  GET complex
---------Count:  8 ----------
MIPS-510.40.20  Kornberg's mediator (SRB) complex
GO:0043529  GET complex
---------Count: 16 ----------
MIPS-220  H+-transporting ATPase, vacuolar
GO:0043529  GET complex
---------Count: 12 ----------
MIPS-510.40  RNA polymerase II holoenzyme
GO:0043529  GET complex
---------Count:  6 ----------
MIPS-370  Protein N-acetyltransferase
GO:0046540  U4/U6 x U5 tri-snRNP complex
---------Count:  6 ----------
MIPS-510.190.110  CCR4 complex
GO:0000274  mitochondrial proton-transporting ATP synthase, stator stalk
---------Count: 12 ----------
MIPS-370  Protein N-acetyltransferase
GO:0005681  spliceosomal complex
---------Count:  6 ----------
GO:0005694  chromosome
GO:0005694  chromosome
---------Count:  6 ----------
MIPS-510.190.110  CCR4 complex
GO:0005694  chromosome
---------Count: 13 ----------
MIPS-370  Protein N-acetyltransferase
```

```
GO:0005694  chromosome
---------Count: 12 -----------
MIPS-360  Proteasome
GO:0005694  chromosome
---------Count: 12 -----------
GO:0005840  ribosome
GO:0005838  proteasome regulatory particle
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
GO:0005840  ribosome
---------Count: 13 -----------
MIPS-360  Proteasome
GO:0005840  ribosome
---------Count:  6 -----------
MIPS-510.190.110  CCR4 complex
MIPS-240.20  HDB complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
MIPS-240.20  HDB complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
MIPS-260.80  Class C Vps protein complex
---------Count:  9 -----------
MIPS-510.190.110  CCR4 complex
MIPS-420.50  F0/F1 ATP synthase (complex V)
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
MIPS-510.190.50  SWI/SNF transcription activator complex
---------Count:  6 -----------
MIPS-370  Protein N-acetyltransferase
MIPS-220  H+-transporting ATPase, vacuolar
```

Finally, we want to know if any of those interactions are statistically significant. To that aim we developed 2 approaches. First, using a graph theory approach, we test whether those interactions are randomly distributed within the interactome.

```
> modelBoeke <- modelSLGI(Boeke2006red,
+           universe= dSLAM, interactome=ScISIC,type="intM", perm=5)
```

A `plot` function allows you the visualize the result. In this case, we note that the number of observed synthetic genetic interaction is globally higher that the simulated data

```
> plot(modelBoeke,pch=20)
```

■echo=FALSE,fig=TRUE■ print(plot(modelBoeke,pch=20))

Note that here, for computer time efficiency, we only performed 5 permutations but for really analysis 100 permutations or more are strongly recommended.

Next, we can perform a Hypergeometric test to identify the multi-protein complexes that presents a unusual number of synthetic genetic interaction.

The `test2Interact` function allows you to summarize the genetic interactions within one cellular organizational unit or between 2 cellular organizational units, taking into account all the interactions tested (positive or negative). One can compute the global interaction matrix as follows:

```
> array <- dSLAM[dSLAM %in% rownames(ScISIC)]
> query <- rownames(Boeke2006)[rownames(Boeke2006) %in% rownames(ScISIC)]
> allInteract <- matrix(1, nrow=length(query), ncol=length(array),
+                dimnames=list(query, array))
> tested <- getInteraction(allInteract, dSLAM, ScISIC)

> testedInteract <- test2Interact(iMat=interact$bwMat, tMat=tested$bwMat, interactome=Sc
> significant <- hyperG(cbind("Tested"=testedInteract$tested,"Interact"=testedInteract$i
+               sum(Boeke),  nrow(Boeke2006red)*length(dSLAM))
```