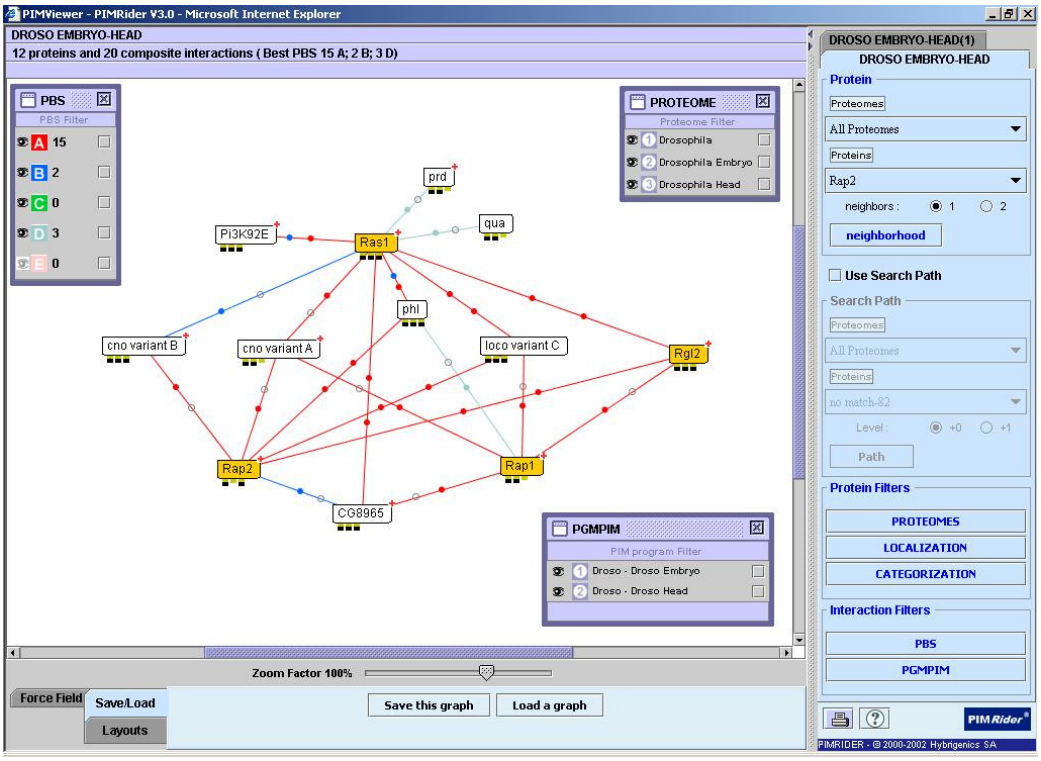
Supplemental Figure 1

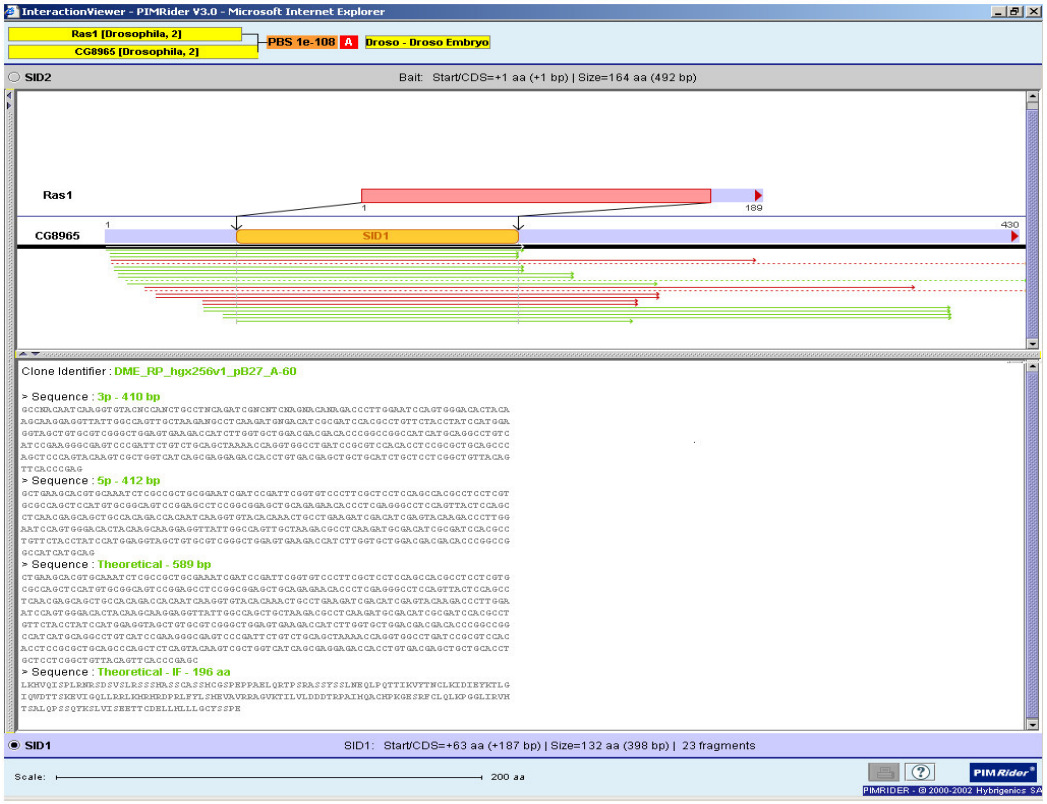
Around Ras: screen shots of the PIMRider, a graphical tool for network exploration.

(A) Part of the protein interaction map surrounding the Drosophila Ras protein as displayed by the PIMViewer. Links between proteins identify physical connections with their color-coded PBS score.
(B) The Interaction Viewer exhibits, for each interaction (here the Ras-CG8965 interaction), the prey fragments found in the screen, their respective sequence and the resulting SID.
(C) DomainViewer for Ras and all its partners displaying, for each protein, the domains and motifs extracted from both experimental (bait and SID) and calculated (transmembrane segments, signal peptides, and functional InterPro domains) analyses.
Notice that comparing networks in vertebrate and flies raises questions about evolution in a perspective different than the one that compares protein sequence conservation and differences. Here Loco as a partner of Ras questions signal transduction evolution. Loco (Locomotion defects), the fly orthologue of RGS14 and RGS12, interacts with Ras and might constitute a molecular link between RTK signaling *via* Ras and GPCR signaling *via* trimeric G-proteins. In fact, Loco interacts actually with both Ras and Rap *via* its RBD (see the PIMRider entry "Rap" in the fly PIM at www.hybrigenics.fr). In vertebrates, RGS14 interacts only with Rap, not with Ras (Traver, S., et al., 2000, *Biochem J* 350 Pt **1:** 19-29). Nothing is documented on RGS12 binding to Ras or Rap but RGS12 carries also two RBD domains. A speculation would be that evolution has split the burden between Ras and Rap to interact with RGS12 and RGS14 respectively. For which respective functions remains to be elucidated.

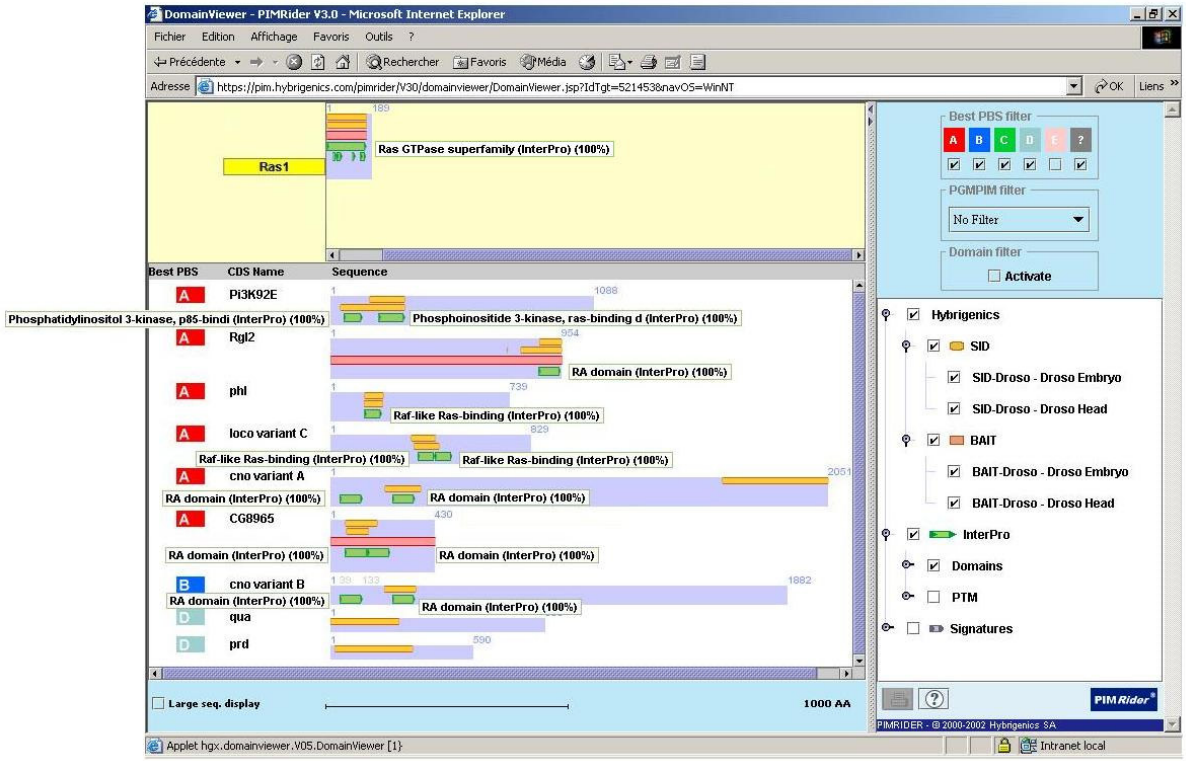
Supplemental Figure 1A



Supplemental Figure 1B



Supplemental Figure 1C



Supplemental Table1 : Bait proteins list

Project	CG	Gene Name or Symbol	Length (Amino acids)	Bait	3AT concentration
Small GTPases					
Ras family	CG9375	Ras1	189	AA 1-164, G12V	none
	CG1956	Rap1	184	AA 1-165, G12V (v1)	none
				AA 1-165, T53A (v2)	none
	CG3204	Rap2	182	full length, G12V, C179S	5mM
	CG2849-RC	RalA	201	AA 1-176, Q69L (252v1)	none
				AA 1-176, T35A (258v1)	none
				AA 1-176, G20V (252v2)	10mM
	CG2849	Ral2	197	full length, G20V	none
	CG8865	Rgl [Rgl2]	954	full length, wild type	0,5mM
	CG11622	RLIP	625	full length, wild type	none
	CG2248	Rac1A	192	AA 1-185	5mM
		Sur-8	677	full length, wild type	none
	CG8604	Amph	602	full length, wild type (v1)	none
				del 292-312 ; del 449-529 (v2)	none
	CG4656	CG4656	826	AA 513-806 (v1)	none
				full-length, wild type (v2)	200mM
	CG8965	CG8965	430	full-length, wild type	0,5mM
	CG11228	hippo [CG11228]	672	full length, wild type (v1)	none
				AA 294-672 (v2)	200mM
ARF6	CG8156	Arf51f [ARF6]	175	full length, Q67L	5mM
	CG31158	CG31158 [EFA6]	900	AA489-734	none
Rab6	CG1418	CG1418 [Pra1]	193	full length, F112L	10mM
	CG6601	Rab6	208	full length, wild type (v1)	0,5mM
Signaling Pathways					
Notch	CG3936	Notch	2703	AA1765-1895 (v1)	10mM
				AA 1896-2109 (v2)	50mM
				AA 2110-2703 (v4)	200mM
	CG3497	Su(H) [Su]	594	full length, wild type	1mM
	CG3619	Delta	832	AA 625-832	none
	CG15010	ago	1326	AA 1-680 (v1)	5mM
				AA 681-1236 (v2)	none
	CG18803	Psn	541	full length, wild type	none
	CG7012	nicastrin	695	full length, wild type	none
	CG18361	dsh	623	full length, wild type	0,5mM
	CG4889	wg	468	full length, wild type	none
	CG8118	mam	1596	AA 1-695 (v1)	100mM
Hedgehog	CG2411	ptc	1286	AA 584-630 (v1)	none
				AA 1120-1230 (v2)	0,5mM
	CG2125	ci	1397	AA 1-1027 (v1)	none
				AA 1-705 (v2)	2mM
	CG6561	fu	805	AA 306-805	0,5mM
	CG8295	Mlf	309	full length, wild type	5mM
	CG6054	Su(fu)	468	full length, wild type	0,5mM
	CG1708	costal-2	1201	full length, wild type (v2)	none
Sprouty	CG1921	sprouty	591	full length, wild type	1mM
Spitz/Gurken	CG10334	spitz	230	AA 161-230	5mM
	CG17610	gurken	294	AA 271-294	none
Membrane and vesicle trafficking					
Exocyst	CG8843	sec5	894	full length, wild type	20mM
	CG5341	sec6	715	full length, wild type	0,5mM
	CG6159	sec10	710	full length, wild type	5mM
	CG7127	exo70	693	full length, wild type	1mM
	CG6095	CG6095 [exo84]	671	full length, wild type	5mM
	CG5462	vartul-2	1247	AA 1-657	none
	CG5462	scrib	1576	AA 1-827	1mM
	CG2671	l(2)gl	1161	full length, wild type	none
SNARES	CG1467	Syx16	352	AA 1-251	1mM
	CG12210	Syb	132	AA 1-110	none
	CG8228	CG8228	574	full-length, wild type	none
TIVAMP	CG1599	Vamp7 [TIVAMP]	218	AA 1-120 (v1)	0,5mM
				AA 1-188 (v2)	0,5mM
Multi vesicular bodies	CG2903	Hrs	760	AA 1-672	2mM
	CG9712	TSG101 [CG9712]	408	full length, wild type	10mM
Centrosome and mitosis					
Centrosome	CG6735	cp309 [AKAP450]	772	AA 912-1109	none
	CG31802	CG31802 [centrin]	186	full-length, wild-type	0,5mM
Polo	CG12306	polo	576	AA 250-576 (v1)	5mM
				AA 2-576 (v2)	none
				AA 294-480 (v3)	none
				AA 480-576 (v4)	none
				AA 380-576 (v5)	none
				AA 2-287 (v6)	none
	CG7186	SAK	769	AA 650-770 (v1)	none
Transcription and cell cycle					
Toy/pax6	CG11186	toy	543	AA 1-325	10mM
Ssu72	CG14216	CG14216 [Ssu72]	195	full length, wild type (v1)	none
				AA 1-105 (v2)	0,5mM
				AA 100-195 (v3)	5mM
Pol D	CG5949	Pol delta	1092	AA 924-1092	20mM
Collier	CG10197	Col	1305	AA 23-527 (v1)	0,5mM

DNA repair and chromatin remodeling					
DNA repair	CG6535	atm	2429	AA 498-998 (v1)	none
				AA 1-520 (v2)	none
				AA 1455-2429 (v3)	none
				AA 975-1475 (v4)	none
				AA 1455-1996 (v5)	none
				AA 1975-2439 (v6)	none
	CG4252	mei41	2354	AA 680-1334 (v2)	none
				AA 1900-2355 (v4)	none
	CG6920	blm	1487	AA 638-1191 (v2)	none
				AA 1120-1488 (v3)	none
	CG5247	Ku70	631	full length, wild type	none
	CG16928	mre11	620	AA 1-381 (v1)	none
				AA 349-620 (v2)	none
				AA 349-616 (v3)	none
				full length, wild type (v4)	none
	CG6754	nbs	811	AA 1-418 (v1)	none
				AA 321-797 (v2)	none
	CG11482	Mlh1	664	full length, wild type	none
	CG6318	Rad51D	250	full lenght, wild type	0,5mM
	CG3325	spn-B	341	full length, wild type	0,5mM
	CG7670	CG7670 [WRN]	353	AA 103-346 (v2)	none
				AA 1-346 (v3)	none
	CG7487	RecQ4	1579	AA 1-420 (v1)	200mM
				AA 798-1100 (v3)	2mM
				AA 1080-1579 (v4)	none
				AA 798-1579 (v5)	none
	CG7948	Rad51	336	full length, wilt type	none
	CG10018	Snm1	763	AA 1-573 (v1)	none
				AA 553-763 (v2)	none
				full length, wild type (v3)	2mM
	CG8169	Pms2	893	AA 1-495 (v1)	none
				AA 470-893 (v2)	0,5mM
	CG6339	rad50	1303	AA 534-1303 (v1)	none
				AA 1-555 (v2)	none
	CG3736	okr	784	AA 483-784 (v1)	none
				AA 1-503 (v2)	none
	CG12176	ligase4 [LigIV]	918	AA 462-918 (v1)	none
				full length, wild type (v2)	none
	CG17227	CG17227 [LigIIIb]	734	full length, wild type	none
	CG4215	spel1	941	del 736-759	none
	CG17269	Fancd2 [CG17269]	1269	AA 1-639	none
Ini1/SNR1	CG1064	Snr1	370	full length, wild type	20mM
Other cellular functions					
Apoptosis	CG8238	Buffy	313	full length, wild type	none
	CG7486	Dredd	366	full length, wild type	none
	CG18188	Damm	255	full length, wild type	none
	CG7788	Ice	339	full length, wild type	none
	CG4319	reaper	65	full length,, wild type	none
	CG4345	grim	138	full length, wild type	none
	CG12284	thread	438	full length, wild type	none
	CG8293	DIAP2	498	full length, wild type	none
	CG6582	Aac11	536	full length, wild type	none
	CG8091	Nc	450	full length, wild type	none
	CG10873	p53	385	AA 45-385	none
	CG3412	Slimb	510	AA 1-199	5mM
Neurexin	CG6827	Neurexin	1284	AA 1240-1284	none
Moesin/Merlin	CG10701	moesin	578	full length, wild type (v1)	none
				AA 1-311 (v2)	50mM
				AA 310-578 (v3)	none
				AA 1-544 (v4)	5mM
				full length, T557A (v5)	none
				full length, T555D (v6)	none
	CG14228	Merlin	635	full length, wild type (v1)	10mM
				AA 1-601 (v2)	200mM
				AA 1-320 (v3)	none
				AA 319-635 (v4)	100mM
				full length, T616A (v5)	5mM
				full length, T616D (v6)	0,5mM
CLIP	CG5020	CLIP-190	1690	full length, wild type	none
Nucleoporins	CG5968	CG5968 [Nup85]	668	full length, wild type	none
	CG5733	CG5968 [Nup133]	1154	full length, wild type	none
Circadian Clock	CG3234	tim	1398	full length, wild type	none
	CG2647	per	1224	full length, wild type	none
	CG3772	cry	542	full length, wild type	none
	CG8727	cyc	413	full length, wild type	none

CG are BDGP 3.1 CG numbers. Alternate gene names used in PIMRider are indicated between brackets. Each screen was first performed on a small scale to define optimal screening conditions. 0, 0.5, 1, 2, 5, 10, 50, 100 and 200mM of 3-aminotriazol were tested.

Supplemental Table 2. Protein-protein interactions shared by the present and Giot et al. studies

CG1	Gene Name or Symbol 1	CG2	Gene Name or Symbol 2	Giot et al. confidence score	PBS score
CG10573	Ko	CG12306	polo	0.3851	D
CG10578	DnaJ-1	CG8295	Mlf	0.3886	A
CG1064	Snr1	CG2168	RpS3A	0.082	A
CG1064	Snr1	CG4609	fax	0.159	A
CG1115	CG1115	CG9712	CG9712	0.9698	A
CG11228	CG11228	CG33193	CG33193	0.6942	A
CG1135	CG1135	CG8965	CG8965	0.28	A
CG11622	RLIP	CG2849	RalA	0.9791	A
CG11718	CG11718	CG8228	CG8228	0.749	D
CG12306	Polo	CG9379	Tensin	0.6976	D
CG13731	CG13731	CG1921	sprouty	0.4332	B
CG14228	Merlin	CG2050	mod	0.3012	A
CG1467	Syx16	CG8228	CG8228	0.9988	A
CG2125	Ci	CG6054	Su(fu)	0.9151	A
CG2903	Hrs	CG6521	Stam	0.6341	A
CG32352	CG32352	CG8604	Amph	0.6379	D
CG3325	spn-B	CG4879	RecQ5	0.5292	D
CG3403	CG3403	CG8965	CG8965	0.1445	A
CG3497	Su(H)	CG5460	H	0.4926	A
CG4557	CG4557	CG6601	Rab6	0.4493	D
CG6213	Vha13	CG6551	Fu	0.5279	D
CG8228	CG8228	CG8506	CG8506	0.4393	B
CG8301	CG8301	CG8965	CG8965	0.4817	D
CG16983	SkpA	CG3412	Slimb	0.4246	A

CG1/2 are BDGP 3.1 CG numbers. Giot et al. considered interactions scored 0.5 and higher as high-confidence interactions.

Supplemental Table 3. Protein-protein interactions shared by the present study and the Flybase genetic interactions.

CG1	Gene Name or Symbol 1	CG2	Gene Name or Symbol 2	PBS Score
CG6829	Ark	CG8091	Nc	D
CG8224	Babo	CG2411	ptc	D
CG2125	Ci	CG15319	nej	D
CG2125	Ci	CG9936	skd	D
CG2534	Cno	CG9375	Ras1	A
CG1708	Costal-2	CG6551	fu	A
CG6551	Fu	CG4637	Hedgehog	D
CG6551	Fu	CG6054	Su(fu)	A
CG4345	Grim	CG13701	skl	D
CG5460	H	CG3497	Su(H)	A
CG3936	Notch	CG9412	rin	D
CG3936	Notch	CG3497	Su(H)	A
CG8091	Nc	CG12284	th	A
CG2647	Per	CG3234	tim	A
CG2845	Phl	CG9375	Ras1	A
CG4141	Pi3K92E	CG9375	Ras1	A
CG17245	plexB	CG2248	Rac1	B
CG2248	Rac1	CG9774	rok	A
CG2248	Rac1	CG2272	slpr	D

CG1/2 are BDGP 3.1 CG numbers.

Supplemental Table 4. Protein-protein interactions shared by the present study and the literature reference set

CG1	Gene Name or Symbol 1	CG2	Gene Name or Symbol 2	PBS score
CG2125	Ci	CG1708	costal-2	A
CG2125	Ci	CG15319	nej	D
CG2125	Ci	CG6054	Su(fu)	A
CG2534	Cno	CG1956	Rap1	A
CG2534	Cno	CG9375	Ras1	A
CG1708	costal-2	CG6551	fu	A
CG12021	Dlt	CG6827	Neurexin	A
CG6551	Fu	CG6054	Su(fu)	A
CG5460	H	CG3497	Su(H)	A
CG3936	Notch	CG3497	Su(H)	A
CG8091	Nc	CG12284	thread	A
CG10295	Pak	CG2248	Rac1	A
CG2647	Per	CG3234	tim	A
CG2845	Phl	CG9375	Ras1	A
CG17245	plexB	CG2248	Rac1	B
CG1956	Rap1	CG8865	Rgl	A
CG2849	RalA	CG11622	RLIP	A
CG9375	Ras1	CG8865	Rgl	A
CG16983	SkpA	CG3412	Slimb	A
CG12210	Syb	CG31136	Syx1A	B

CG1/2 are BDGP 3.1 CG numbers.

Supplemental Table 5. Protein-protein interactions confirmed by co-immunoprecipitation and/or pull-down experiments.

PBS	Tested	Confirmed
A	18	15 (83%)
B	6	4 (67%)
C	5	4 (80%)
D	7	2 (29%)
ABC	29	23 (79%)
ABCD (Total)	36	25 (69%)

Supplemental Table 6. Estimation of Y2H screening reproducibility.

Bait	Prey fragments (screen A)	Prey fragments (screen B)	Common preys fragments / total prey fragments (screen A+B)
Ras1	163	176	336/339 (99%)
Rap2	194	319	484/513 (94%)
Slimb	142	292	368/434 (85%)

For the 3 indicated Drosophila baits, the prey fragments identified in 2 independent screens of the Drosophila embryo cDNA library were compared. The number of fragments coding for common preys was divided by the total number of prey fragments identified in both screens.

Supplemental Method: Predicted Biological Score (PBS®)

Introduction

The general strategy to identify potentially biologically significant interactions from yeast two-hybrid screens is to compute a predictive score for every single interaction based on experimental data. This score is referred to as the PBS®, or Predictive Biological Score. It is a statistical score relying on two different levels of analysis: firstly a local score taking into account the detailed results of a screen is computed for each interaction, and secondly, a global score is computed from the local scores by integrating results from all screens performed with the same library. As a consequence a local score is fixed when the corresponding screen had been completed, whereas global scores are computed incrementally as screening results are added to our knowledge database. Prior to the PBS computations, the distribution of fragments in the library and of overlapping prey fragments within screens must be determined:

Prior analysis #1: library fragment distribution

The distribution of fragments in prey libraries can be correctly determined only by randomly picking and sequencing a number of clones from the library allowing several times the coverage of the genome or, alternatively, by normalizing the library. Regarding the library calibration, this is intractable in practice for all but the smallest genomes (such as viruses).
Two different approximations are used depending on the prey library type, 'genomic' (derived from genomic DNA of viruses, prokaryotes or lower eukaryotes like yeast) or 'cDNA' (derived from RT-PCR of higher eukaryote mRNA):

i. Genomic prey libraries
Genomic prey libraries are built through mechanical, theoretically unbiased, breakage of genomic DNA. They are characterized by one number and two distributions :
- N_{ind} the number of independent fragments in the library: this number is approximated during the library construction process ; basically for Hybrigenics' library it is around 2 millions ;
- f_{size} the distribution of fragment size: this is experimentally determined by random sequencing of 100 to 200 prey fragments ;
- f_{start} the distribution of fragment start positions in the genome. This distribution is approximated by a uniform distribution:

$$f_{start}(x) = \frac{1}{s_g}$$

where s_g is the size of the genome from which the library is built from, and x is a nucleotide position in the genome. Regarding the way genomic libraries are built, this uniform f_{start} distribution is theoretically exact.

ii. cDNA prey libraries
These prey libraries are built from oligo(dT)- or random-primed reverse transcribed mRNA. If one can estimate and use the previously defined N_{ind} and f_{size} parameters to characterize the cDNA fragment distribution in such libraries, the f_{start} distribution is however almost impossible to correctly approximate. Indeed, the same distribution (using an approximation of the transcriptome size – basically the sum of lengths of all transcripts – for s_g) is false because of significant differences in mRNA representation in tissues and biases in cDNA synthesis.
We therefore prefer to use a lower grain approximation and characterize the fragment distribution in cDNA prey libraries only by a single distribution, $f_{presence}$, which represents the distribution of transcript occurrences in the library. This simpler distribution is still hard to define exactly because of the aforementioned variations of mRNA expression levels. As a complete characterization of transcript distribution would require random picking, sequencing and unambiguous identification of a high number of prey fragments, we approximate $f_{presence}$ by an uniform distribution:

$$f_{presence}(T) = \frac{1}{N_T}$$

where T is a given transcript and N_T is the total number of different transcripts in the library. This last parameter is initially approximated from literature data and eventually refined as additional transcripts are identified during library two-hybrid screening.
This hypothesis holds true for about 80% of transcripts and is used for simplicity's sake as well as to avoid the prohibitive cost of a full library calibration. But it is obviously a false approximation for very rare as well very abundant mRNA. This must be kept in mind for the results analysis (see the paragraph 'PBS interpretation' below).

Prior analysis #2: fragment distribution and gene identification

For each yeast two-hybrid screen, 5' and 3' sequences of all positive clones are determined and filtered by using PHRED (Ewing and Green 1998) and by masking ALU repeats. Sequence contigs are then built using CAP3 (Huang and Madan 1999) and compared to one or several reference database(s) using BLASTN (Altschul et al. 1997). A reference database can be an organism-specific database, such as GadFly for Drosophila or SGD for yeast, or a generic database such as the latest release of GenBank. If entries corresponding to the complete mRNA are found, the best annotated entry is assigned to every overlapping prey fragment family. The SID® (Selected Interacting Domain) is the common part of all overlapping fragments in a family. This region contains the domain that interacts with the bait. Each two-hybrid screening experiment generates a list of bait-SID interactions. Cardinalities for one screen are:
- 1 bait
- n SIDs assigned to m genes, with $n \geq m$ (several distinct fragment families may be assigned to the same gene).

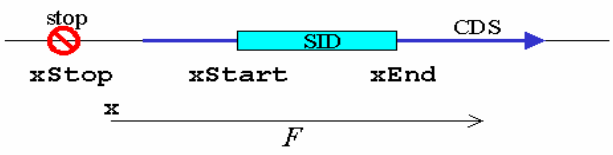
Local PBS computation

Each fragment family is first analyzed in terms of coding capabilities (antisense and out-of-frame fusion fragments). The prey fragment families which have no or very improbable biological coding capability are then discarded:
- families containing only antisense fragments ;
- families containing only out-of-frame fusion fragments selected in a single frame.
Families containing several fragments in different frames (in-frame and out-of-frame or out-of-frame in the two non-coding frames) are kept for further analysis because we consider they encode valid biological polypeptides thanks to translational frameshift events which occur in yeast.

The local score is computed as an E-value for each remaining fragment family, by comparing observed results to a theoretical random background: the fragment distribution is compared to an expected distribution based on a statistical model of the two-hybrid experiment mechanism and calibrated by the specific prey library characteristics. This step is performed in two sub-steps.
* First, for each overlapping fragment family, that is for each SID, we calculate the probability p that a fragment F randomly drawn from the library contains the SID.
For genomic libraries, p is calculated as follows:

$$p = \int_{x=xStop}^{xStart} \int_{s=xStart-x+1}^{+\infty} f_{start}(x) f_{size}(s) dx ds$$

where:
- *xStart* is the start position of the SID ;
- *xStop* is the position of the first STOP codon upstream and in frame with the CDS containing the SID ;
- f_{start} and f_{size} are the genomic prey library distributions defined above ;
- variables x and s represent the start and the size of the fragment F, respectively:



For cDNA libraries, p is simply approximated as follows:

$$p = f_{presence}(T)$$

where:

- $f_{presence}$ is the cDNA distribution defined above;
- T is the transcript containing the SID.

* Second, for each fragment family or SID, we calculate the PBS as the probability to pick randomly from the library at least the number n of overlapping fragments containing the SID (each having the probability p defined above) out of the N fragments identified in the screen:

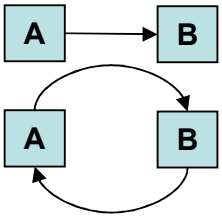
$$PBS = \sum_{X=n}^{N} C_N^X p^X (1-p)^{N-X}$$

So this local PBS value represents the probability of a bait-SID interaction being non-specific. It measures how significantly different the profile of overlapping fragments is from a theoretical background noise representing a completely non-specific selection (simulated by the random drawing of fragments from the library).

Global PBS computation

The PIM® (Protein Interaction Map) is then built by pooling all the bait-SID interactions from several screens. The result is a graph where vertices (nodes) are proteins and edges are protein-protein interactions, defined by one or several different bait-SID interactions.

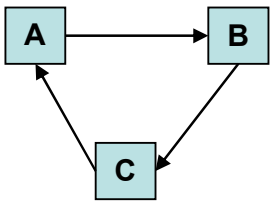
The global PBS is computed from local PBS in two steps:
- the global connectivity of the interaction map is analyzed to mark highly connected prey polypeptides (SIDs which are found as prey with frequency above a fixed threshold). Note that this step tags domains, rather than whole proteins, as potentially “sticky”. In that case, the local PBS of the bait-sticky_SID interaction is set to 1.
- local E-values are combined when the same protein pair is involved, assuming that bait and prey fragments overlap for both proteins:



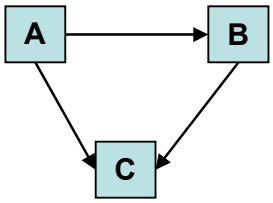
$$GlobalPBS_{A-B} = LocalPBS_{A\to B}$$

$$GlobalPBS_{A-B} = LocalPBS_{A\to B}.LocalPBS_{B\to A}$$

The interaction map is searched for 3-cycles (i.e. small connectivity patterns linking 3 proteins) and PBS may be increased if they mimic probable biologically relevant networks. For examples:



Indirect Rebound :
$PBS_{A\to B}$ increases
$PBS_{B\to C}$ increases
$PBS_{C\to A}$ increases



Bait interacts with 2 interacting preys
$PBS_{A \rightarrow B}$ increases
$PBS_{A \rightarrow C}$ increases

In conclusion, the PBS score reflects the probability that an interaction is found by chance. It ranges from 0 to 1, but is grouped in five categories (A, B, C, D, and E) for user convenience. Inter-category thresholds are chosen manually with respect to a training data set containing known true-positive and false-positive interactions (not shown): A < 1e-10 < B < 1e-5 < C < 1e-2.5 < D < 1. The E category gathers scores equal to 1.

PBS interpretation

PBS category	Interpretation
A B C	These interactions are technically very reliable. They correspond to interactions found in two reciprocal and independent screens (A->B and B->A) or interactions found in a single screen with many overlapping prey fragments.
D	Basically these interactions are defined by a single bait-SID interaction, the SID being defined by a singleton fragment instead of a family of several overlapping fragments. This category is the hardest to analyze because it mixes two classes of interactions: - false-positive interactions (background noise): one singleton fragment has been selected by chance by the bait (non-specific selection) - interactions hardly detectable by two-hybrid systems because of conformation, toxicity in yeast, very low representation of the mRNA in tissue (rare mRNAs, see above) etc… This class of interactions is potentially very interesting because Hybrigenics' PIM technology is the only one able to detect them.
E	These interactions involve SID that have non-specifically been found as prey in many independent screens. They are likely to be false-positives of the two-hybrid system.