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Figure S1:

Power-law distributions for two promiscuity measures in 27 contemporary and ancestral eukaryotic genomes. Each panel shows the distributions of domain promiscuity measures on a log-log scale; domain abundance (blue) and domain degree in the bigram network (red) in a genome. Also shown are the regression coefficients and squared multiple correlation coefficients as well as the Pearson linear correlation coefficients. Names of the species are shown on the top of each panel.

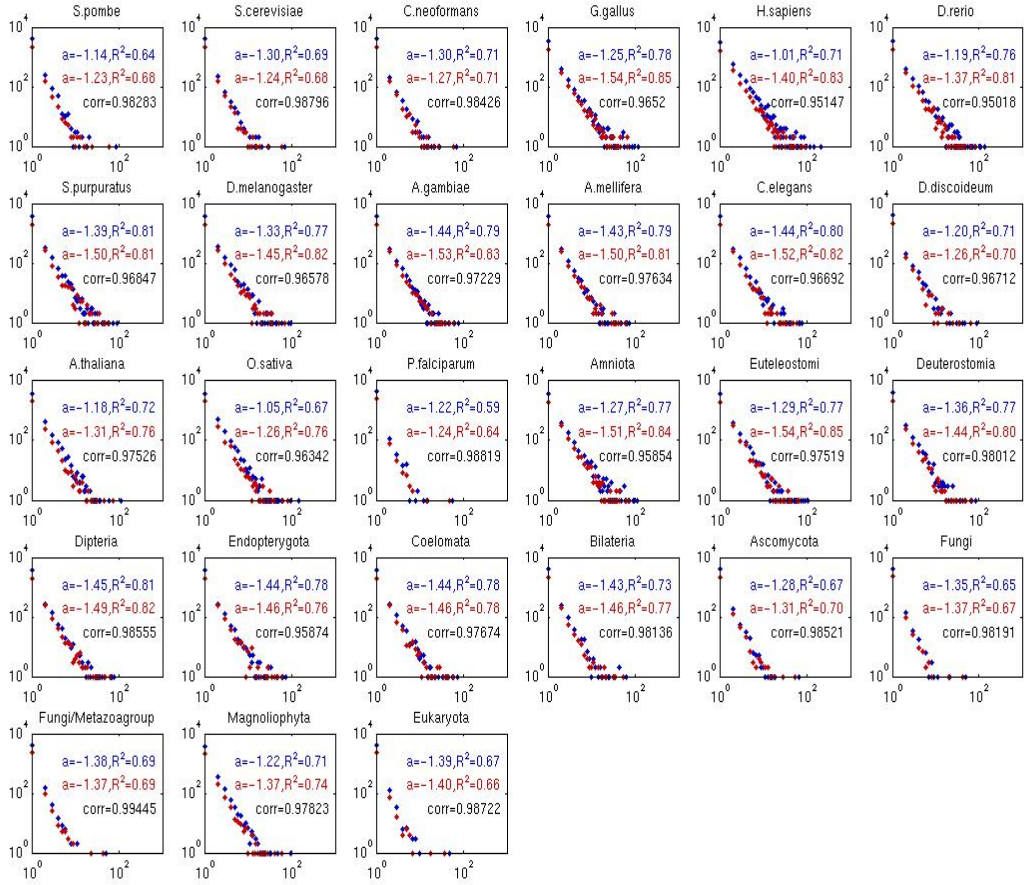

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Figure S2:

Fraction of domains (A, C) and domain clusters (B,D) with the maximum promiscuity rate on a given branch. Domain promiscuity is maximal along a given branch if its rate of promiscuity increase along this branch is higher than along any other branch in the tree.

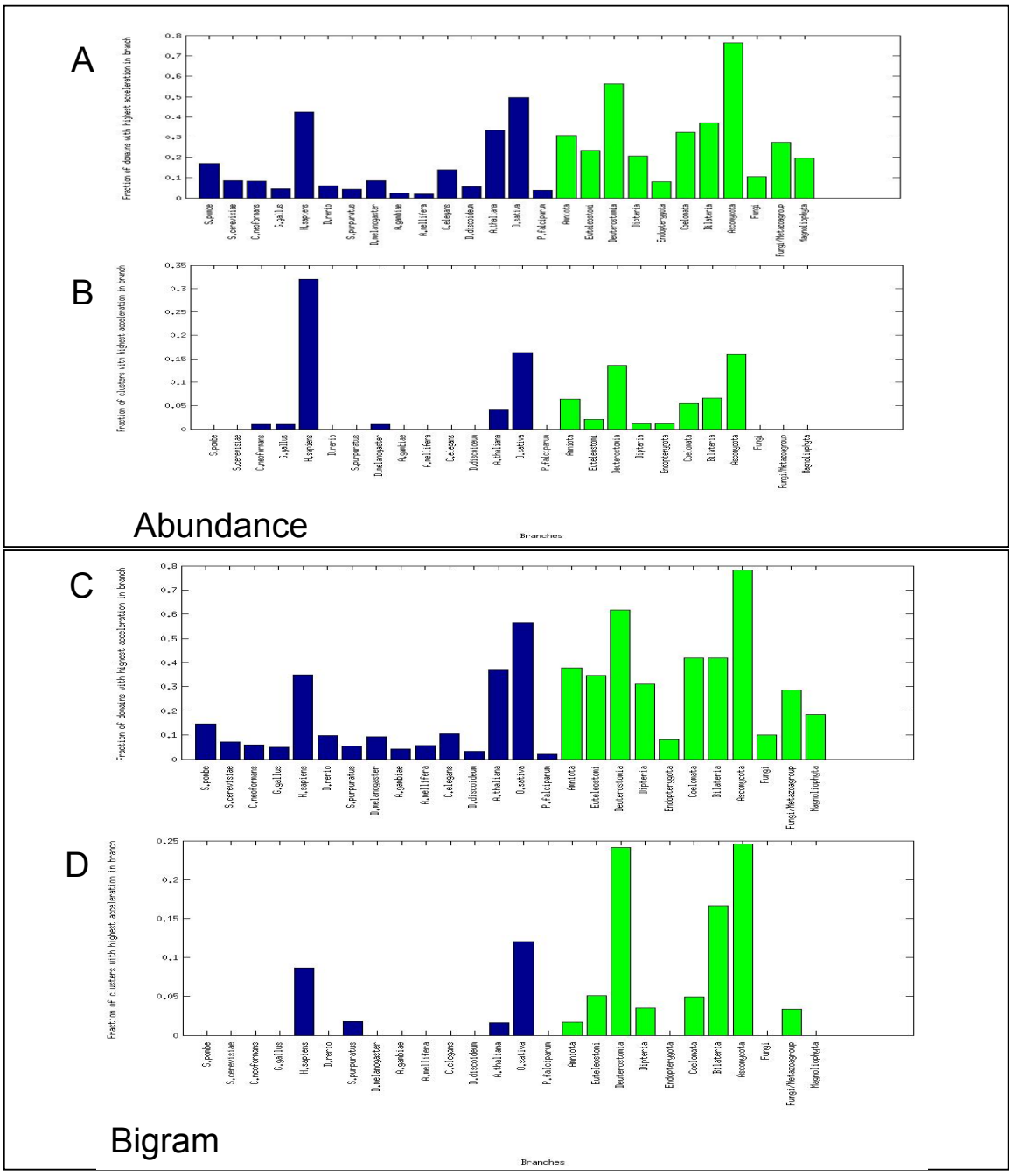

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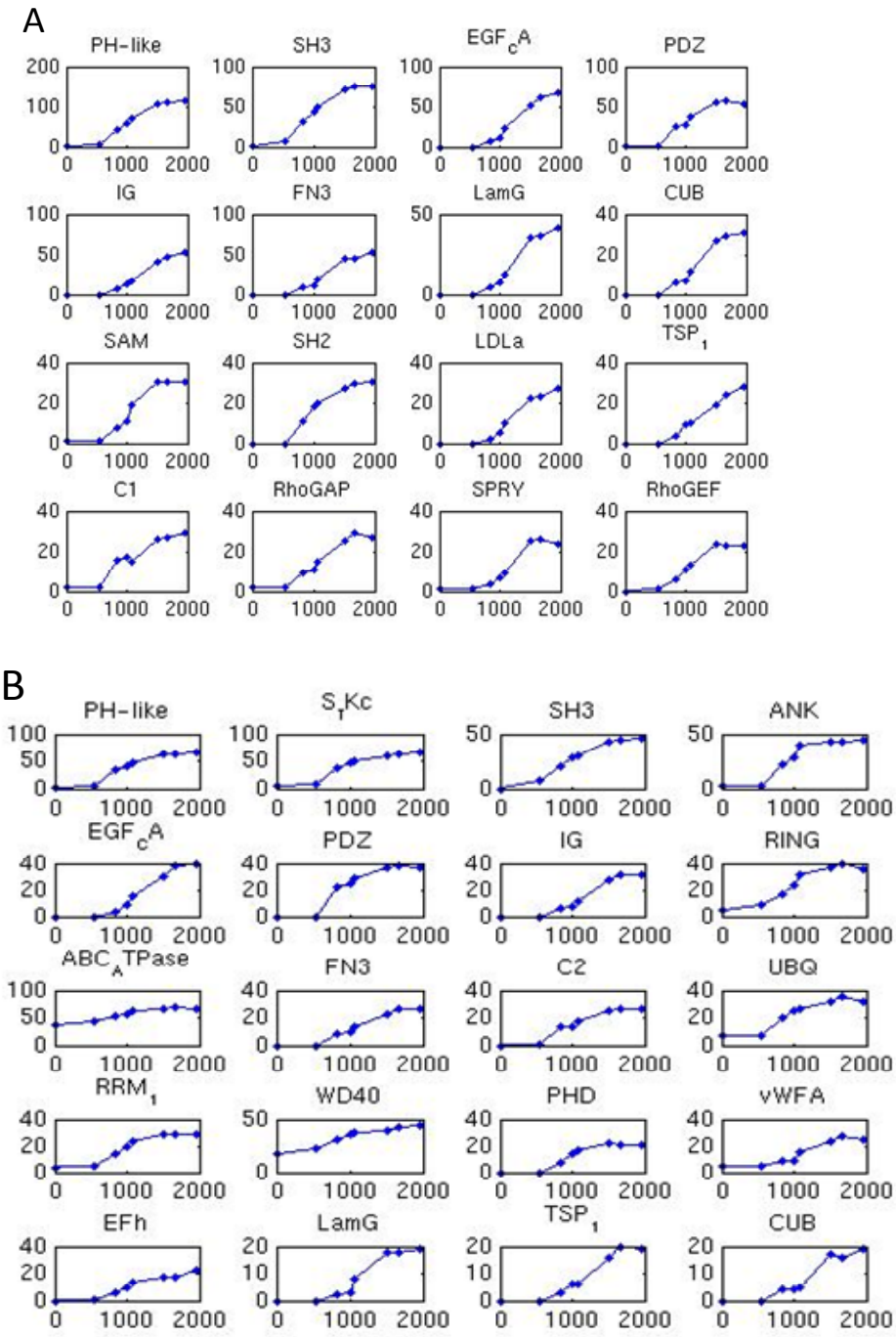
Figure S3:

Evolution of domain promiscuity in animals. X axis represents cumulative time from the root of the tree. Y axis represents the domain promiscuity in the corresponding ancestral genome. Shown are top tenth percentile domains with significant linear correlation between promiscuity and evolution time in the different genomes. Promiscuity measures are: A. abundance, B. degree in the bigram network..

G. gallus:



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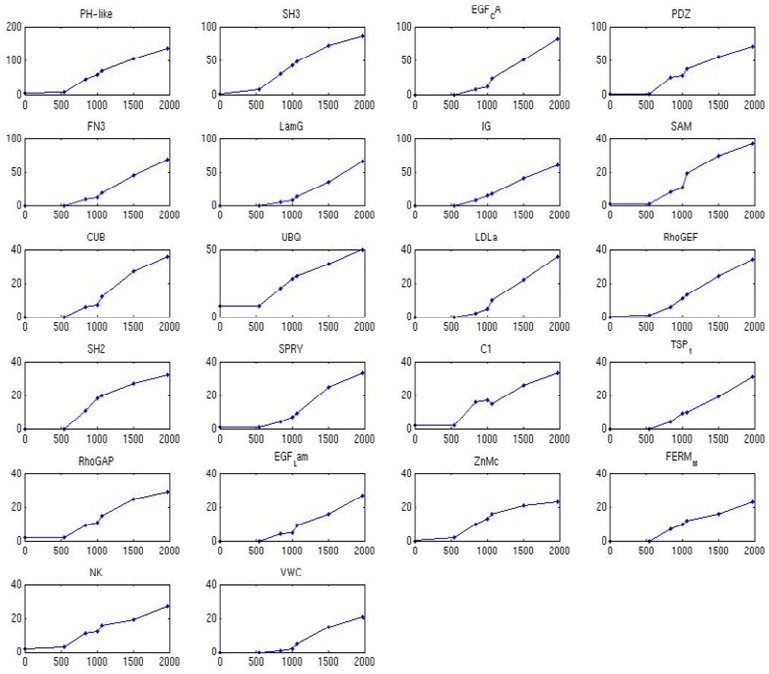
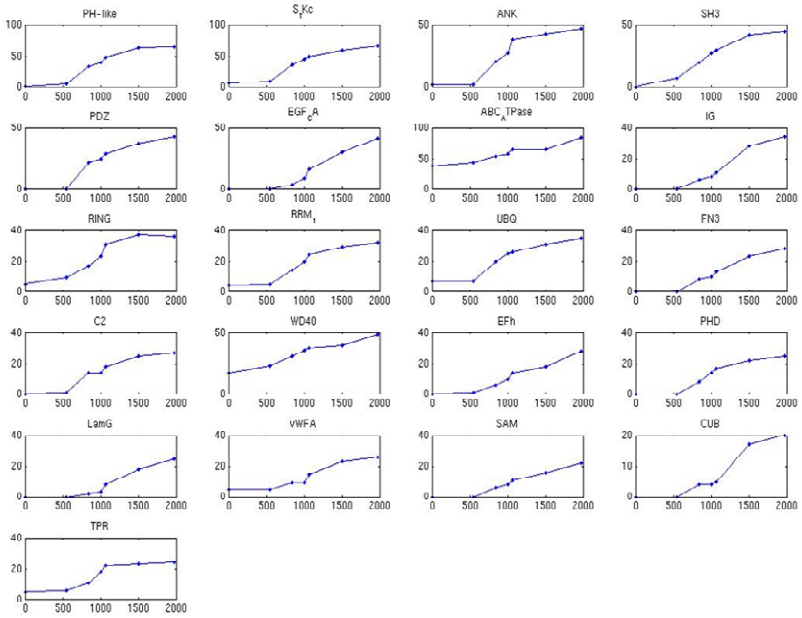
D. rerio:

A



B



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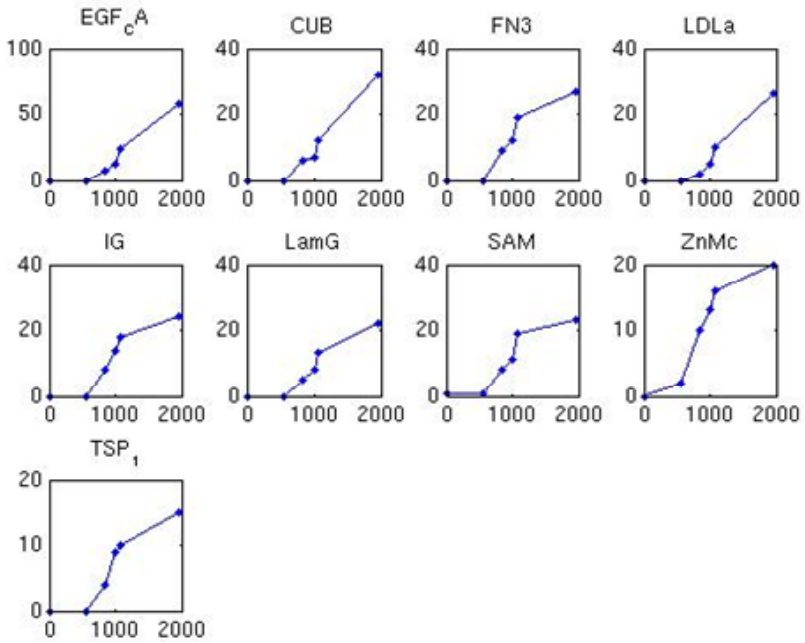
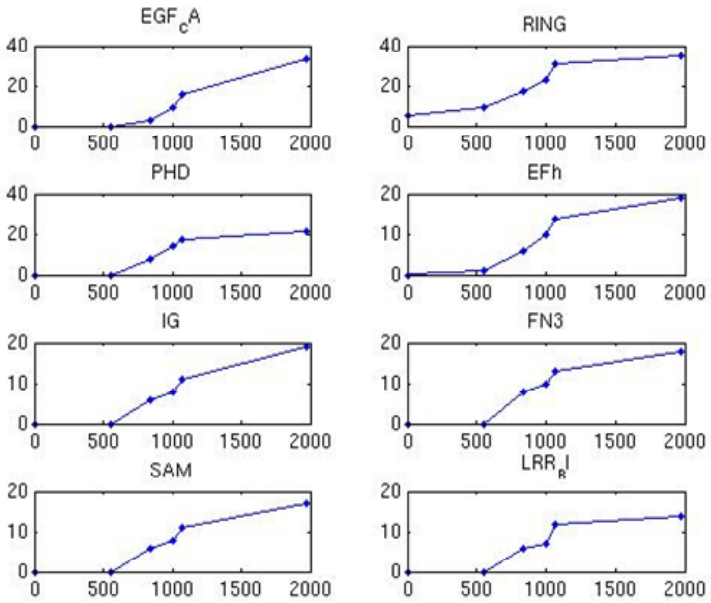
S. purpuratus

A



B



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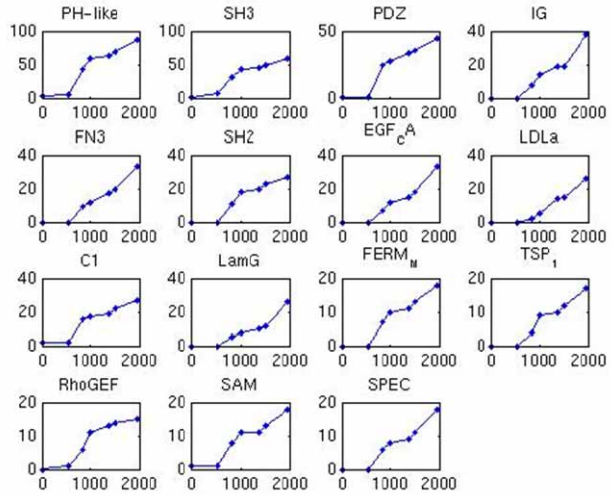
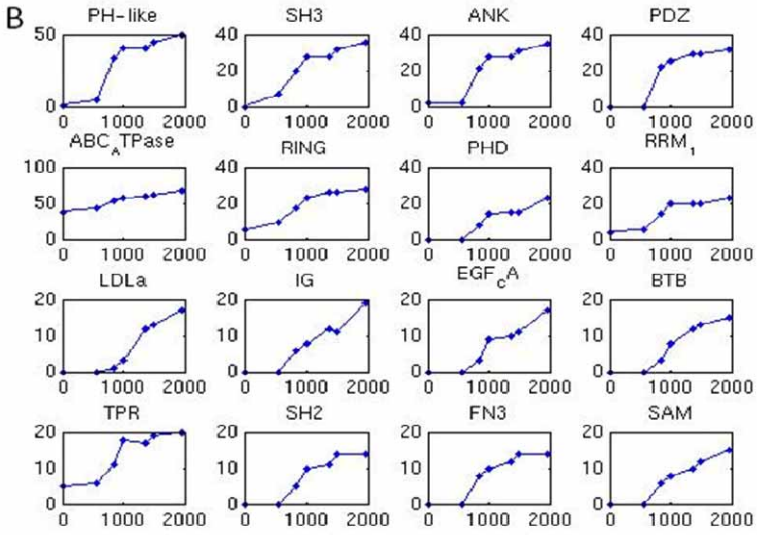
D. melanogaster

A



B



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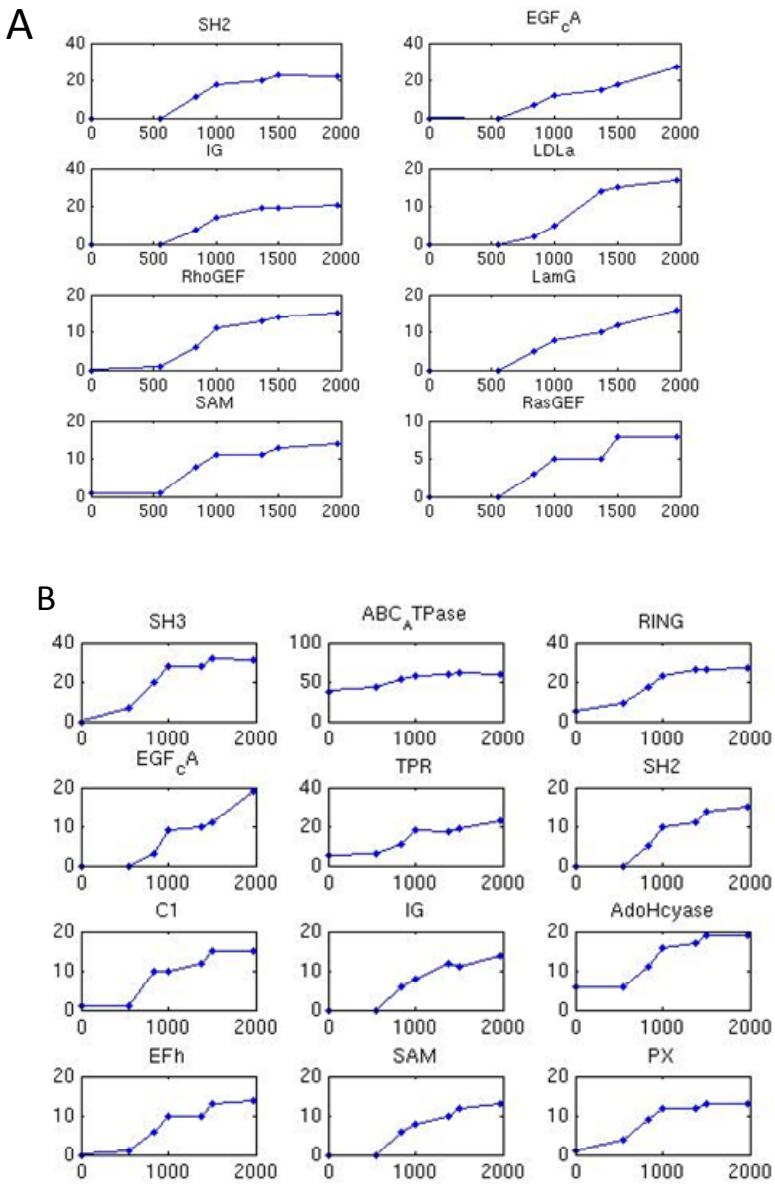
A. gambiae:



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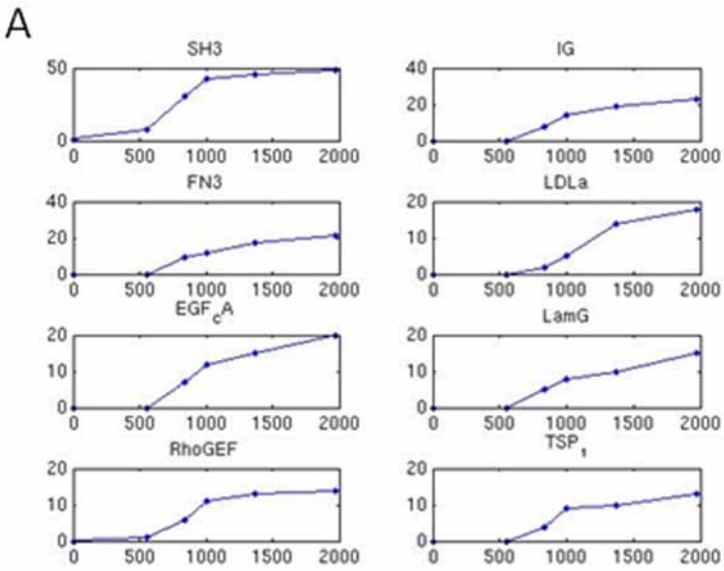
A. mellifera:



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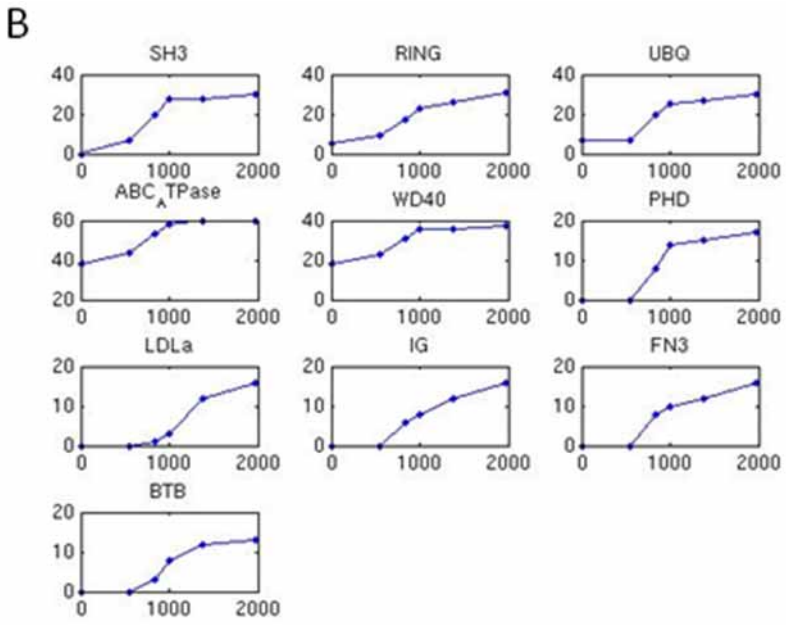

Figure S4:

Evolution of domain promiscuity in Bilaterians. Shown are representative domains having roles in the formation of embryonic body pattern.

Legend:

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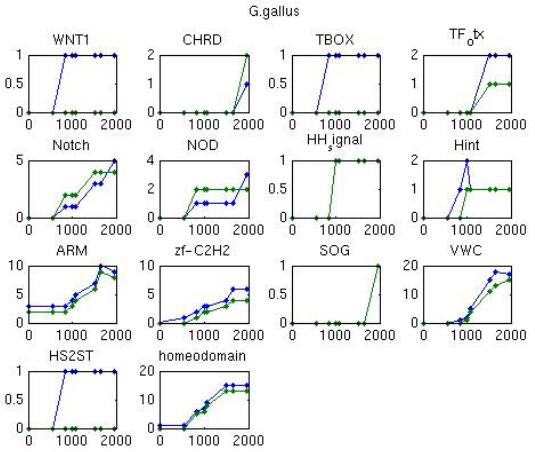

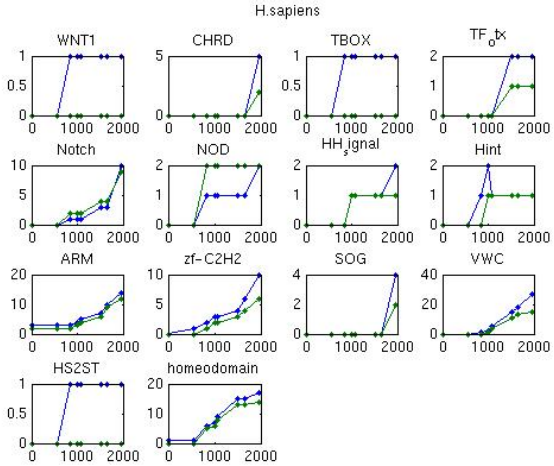

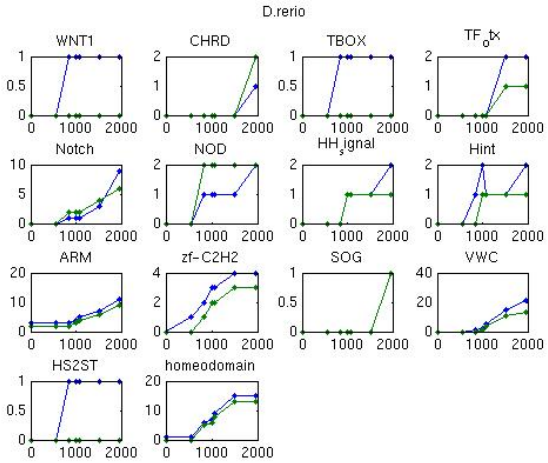

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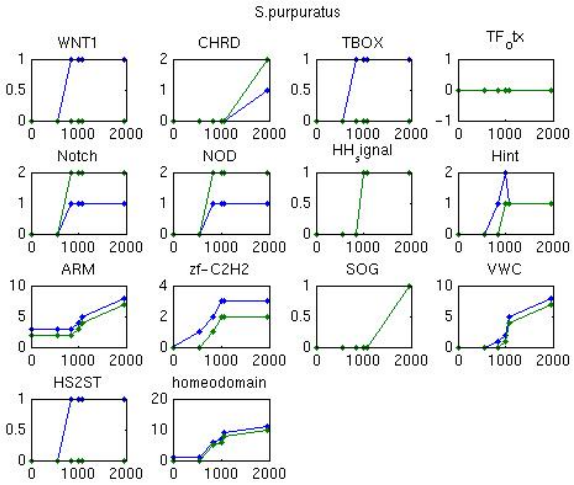

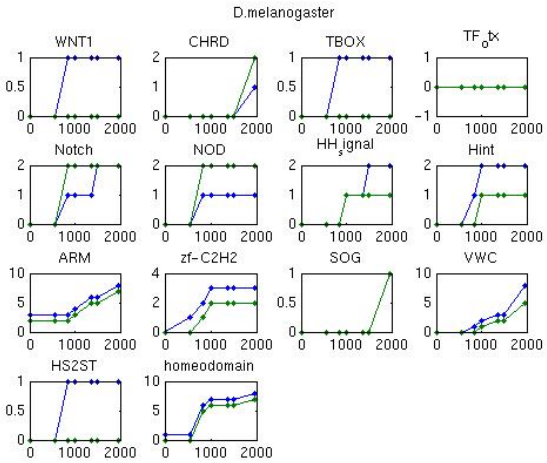

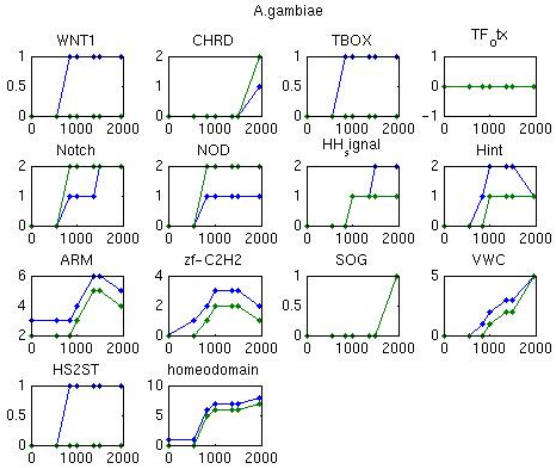

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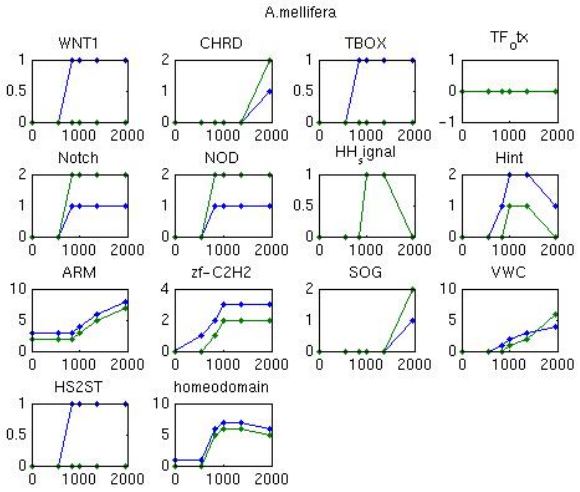

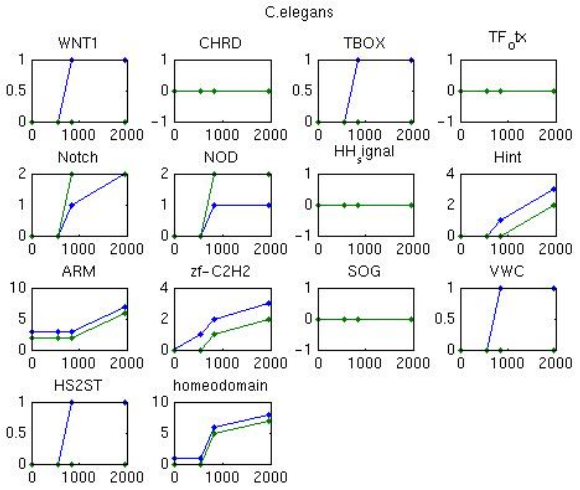

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Table S1:

Table summarizing the promiscuity measures of eukaryotic domains used in Figure 3, and their presence/absence in prokaryotes. 7 domains out of the pool of 33 domains in figure 3 are found in prokaryotes but are not inferred to be present in the internal Eukaryotes node in our data (shown in bold).

Domain	Abundance promiscuity in Eukaryotes	Bigram promiscuity in Eukaryotes	Presence in Prokaryotes, according to our data
PH-like	3	1	-
SH3	1	0	+
PDZ	1	0	+
ANK	3	2	+
LamG	0	0	+
CUB	0	0	+
C1	2	1	-
RhoGEF	0	0	+
SH2	0	0	-
SAM	1	0	+
RhoGAP	2	1	+
SPRY	1	0	+
ZnMc	0	0	+
FERM_N	0	0	-
BBC	0	0	-
VWC	0	0	-
S_TKc	8	6	+
EGF_CA	0	0	-

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IG	0	0	+
ABC_ATPase	47	38	+
RING	5	5	+
UNQ	8	7	+
FN3	0	0	+
WD40	18	18	+
RRM_1	5	4	+
C2	1	0	-
vWFA	7	5	+
PHD	1	0	-
EFh	1	0	+
TPR	6	5	+
TSP_1	0	0	-
LRR_RI	1	0	+
NHL	0	0	+

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Table S2:

Functional GO annotation for the top 10% of domains with significant linear correlation between promiscuity and evolutionary time in different genomes.

Species\promiscuity	Abundance	Bigram
S. cerevisiae		
S. pombe		
C. neoformans		
G. gallus	small GTPase mediated signal transduction regulation of Rho protein signal transduction regulation of Ras protein signal transduction regulation of small GTPase mediated signal transduction	autophagic vacuole formation sulfate assimilation biosynthetic process cell killing metabolic process DNA replication mismatch repair protein modification process ubiquitin cycle sulfur utilization cell cycle chromosome segregation integrin-mediated signaling pathway biosynthetic process transport protein ubiquitination protein modification by small protein conjugation biopolymer modification
H. sapiens	small GTPase mediated signal transduction regulation of Rho protein signal transduction regulation of Ras protein signal transduction regulation of small GTPase mediated signal transduction	autophagic vacuole formation sulfate assimilation cell killing metabolic process biosynthetic process mismatch repair protein modification process ubiquitin cycle sulfur utilization transport cell cycle chromosome segregation protein modification by small protein conjugation biopolymer modification intracellular transport Golgi vesicle transport establishment of localization in cell
D. rerio		
S. purpuratus	intracellular signaling cascade	
D. melanogaster	intracellular signaling cascade regulation of Rho protein signal transduction	
A. gambiae	small GTPase mediated signal transduction regulation of signal transduction regulation of Rho protein signal transduction regulation of Ras protein signal transduction regulation of small GTPase	

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	mediated signal transduction	
A. mellifera	regulation of signal transduction regulation of Rho protein signal transduction regulation of Ras protein signal transduction regulation of small GTPase mediated signal transduction	autophagic vacuole formation transport
C. elegans		
D. discoideum		
A. thaliana		
O. sativa		
P. falciparum		

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Table S3:

Correlation between domain promiscuity and time passed from the root of the tree. This table summarizes the data used to analyze the change of domain promiscuity along different evolutionary pathways.

		Abundance	Bigram
Significantly correlated domains with time		1587	878
Significantly linearly correlated, R^2>0.8		607	329
Significantly linearly correlated only on the path leading to the genome:	*S. pombe*	3	4
	S. cerevisiae	4	4
	C. neoformans	0	0
	G. Gallus	168	197
	H. sapiens	168	226
	D. rerio	212	204
	S. purpuratus	86	76
	D. melanogaster	150	154
	A. gambiae	76	115
	A. Mellifera	76	96
Domains which have signaling functions, out of the top ten percentile of the genome:	*S. pombe*	0	0
	S. cerevisiae	0	0
	C. neoformans	0	0
	G. Gallus	3 (33%)	4 (36%)
	H. sapiens	3 (30%)	4 (36%)
	D. rerio	4 (36%)	4 (36%)
	S. purpuratus	1 (33%)	1 (25%)
	D. melanogaster	3 (37%)	1 (12%)
	A. gambiae	2 (40%)	2 (29%)
	A. Mellifera	2 (66%)	1 (20%)

Supplementary Material (ESI) for Molecular BioSystems

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