Supplemental Information

Dynamic coupling and allosteric networks in the alpha subunit of heterotrimeric G proteins

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Table S1. Analyzed crystallographic structures of G protein α subunit.

PDB ID	Chain	Ligand	Source	Resolution	Reference
1FQJ	A, D	ALF, GDP, MG	*Bos Taurus*	2	Slep et al. (2001)
1FQK	A, C	ALF, GDP, MG	*Bos Taurus*	2.3	Slep et al. (2001)
1GOT	A	MSE, GDP	*Bos Taurus*	2	Lambright et al. (1996)
1TAD	A, B, C	ALF, CA, CAC, GDP	*Bos Taurus*	1.7	Sondek et al. (1994)
1TAG	A	GDP, MG	*Bos Taurus*	1.8	Lambright et al. (1994)
1TND	A, B, C	CAC, GSP, MG	*Bos Taurus*	2.2	Noel et al. (1993)
3V00	A, B, C	GDP	*Bos Taurus*	2.9	Singh et al. (2012)
1AGR	A, D	ALF, CIT, GDP, MG	*Rattus Norvegicus*	2.8	Tesmer et al. (1997)
1AS0	A	GSP, MG, SO4	*Rattus Norvegicus*	2	Raw et al. (1997)
1AS2	A	GDP, PO4	*Rattus Norvegicus*	2.8	Raw et al. (1997)
1BH2	A	GSP, MG	*Rattus Norvegicus*	2.1	Posner et al. (1998)
1CIP	A	GNP, MG	*Rattus Norvegicus*	1.5	Coleman et al. (1999)
1GFI	A	ALF, GDP, MG	*Rattus Norvegicus*	2.2	Coleman et al. (1994)
1GG2	A	GDP	*Rattus Norvegicus*	2.4	Wall et al. Cell (1995)
1GIA	A	GSP, MG	*Rattus Norvegicus*	2	Coleman et al. (1994)
1GIL	A	GSP, MG	*Rattus Norvegicus*	2.3	Coleman et al. (1994)
1GIT	A	GDP, PO4	*Rattus Norvegicus*	2.6	Berghuis et al. (1996)
1GP2	A	GDP	*Rattus Norvegicus*	2.3	Wall et al. (1995)
1KJY	A, C	CS, GDP, MG	*Homo Sapiens*	2.7	Kimple et al. (2002)
1SVK	A	ALF, GDP, MG	*Rattus Norvegicus*	2	Thomas et al. (2004)
1SVS	A	GNP, MG	*Rattus Norvegicus*	1.5	Thomas et al. (2004)
2GTP	B	ALF, GDP, MG	*Homo Sapiens*	2.5	Soundararajan et al. (2008)
2IHB	A	ALF, GDP, MG	*Homo Sapiens*	2.7	Soundararajan et al. (2008)
2ODE	A, C	ALF, GDP, MG	*Homo Sapiens*	1.9	Soundararajan et al. (2008)
2OM2	A, C	GDP, MG	*Homo Sapiens*	2.2	Sammond et al. (2007)
2V4Z	A	ALF, GDP, MG	*Homo Sapiens*	2.8	Kimple et al. (2009)
2XNS	A, B	GDP, SRT,	*Homo Sapiens*	3.4	Sammond et al.

		SO4			(2011)
2ZJY	A	ALF, GDP, MG	*Rattus Norvegicus*	2.8	Morikawa et al. To be published
3C7K	C	ALF, GDP, MG	*Mus Musculus*	2.9	Slep et al. (2008)
3FFA	A	GSP, MG, SO4	*Rattus Norvegicus*	2.3	Kapoor et al. (2009)
3ONW	A, B	GDP, SO4	*Homo Sapiens*	2.4	Bosch et al. (2011)
3QE0	B	GDP, MG	*Homo Sapiens*	3	Bosch et al. (2012)
3QI2	A, B	GDP, GOL, SO4	*Homo Sapiens*	2.8	Bosch et al. (2012)
4G5O	A, D	CIT, GDP, SO4	*Homo Sapiens*	2.9	Jia et al. To be Published
4G5Q	A, D	GDP, SO4, CIT	*Homo Sapiens*	2.9	Jia et al. To be Published
4G5R	A	GDP, SO4, CIT	*Homo Sapiens*	3.5	Jia et al. To be Published

Table S2. Normalized node degeneracy from path analysis of correlation networks derived from MD simulations. For each network, 500 suboptimal paths were calculated. Nodes with degeneracy≥0.1 in one or more networks are shown and corresponding degeneracy values are colored in red, green and blue, respectively, for GTP, GDP and GDI state networks. Source and sink nodes are highlighted in gray.

Paths from α5 to γ-Pi binding site

SSE[a]	β1				PL		α1	SI		β2	β3		
Residue	K31	L32	L33	L34	K42	S43	T44	T177	T178	I180	R193	M194	F195
GTP	0.51	0.70	0.36	0.11	0.00	0.01	0.00	0.25	0.18	0.17	0.21	0.31	0.64
GDP	0.00	0.00	0.00	0.00	0.89	0.47	0.94	0.00	0.00	0.00	0.00	0.00	0.00
GDI	0.00	0.00	0.00	0.00	0.02	0.70	0.99	0.00	0.00	0.00	0.00	0.00	0.00
Entropy[b]	0.66	0.89	0.90	0.84	0.83	0.85	0.86	0.82	0.48	0.80	0.42	0.81	0.55

SSE	SII			L10		α5							
Residue	D196	V197	G198	T323	D324	Q326	N327	V328	K329	F330	V331	F332	D333
GTP	0.58	0.54	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GDP	0.09	0.07	1.00	0.91	0.95	0.39	0.69	0.10	0.57	0.37	0.23	0.67	0.22
GDI	0.85	0.94	1.00	0.95	0.83	0.31	0.78	0.05	0.17	0.52	0.44	0.50	0.17
Entropy	0.79	0.70	0.83	0.55	0.70	0.25	0.35	0.64	0.25	0.11	0.52	0.56	0.18

SSE	α5					
Residue	A334	V335	T336	D337	I338	I339
GTP	0.00	0.00	0.00	0.00	0.00	1.00
GDP	0.05	0.49	0.67	0.15	0.52	1.00
GDI	0.20	0.34	0.60	0.05	0.15	1.00
Entropy	0.18	0.69	0.24	0.49	0.34	0.74

Paths from β1 to RasD-HD interface

SSE	β1				PL		α1		LE			αF	
Residue	K31	L32	L33	L34	K42	S43	T44	K47	N145	D146	S147	L171	R172
GTP	1.00	0.37	0.31	0.06	0.02	0.19	0.00	0.00	0.00	1.00	0.00	0.00	0.02
GDP	1.00	0.38	0.40	0.44	0.43	0.86	0.33	0.15	0.04	1.00	0.67	0.16	0.63
GDI	1.00	0.10	0.14	0.11	0.00	0.00	0.00	0.00	1.00	1.00	0.00	0.00	0.00
Entropy	0.66	0.89	0.90	0.84	0.83	0.85	0.86	0.80	0.07	0.83	0.27	0.82	0.48

SSE	SI							β2					β3
Residue	S173	R174	V175	K176	T177	T178	G179	I180	I181	E182	T183	Q184	N191
GTP	0.00	1.00	0.67	0.57	0.69	0.16	0.00	0.06	0.00	0.00	0.00	0.00	0.00
GDP	0.65	0.85	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.02	0.00	0.01
GDI	0.00	1.00	0.81	0.57	1.00	0.68	0.65	0.51	0.39	0.36	0.31	0.18	0.16
Entropy	0.24	0.63	0.35	0.31	0.82	0.48	0.84	0.80	0.21	0.55	0.24	0.20	0.11

SSE	β3			SII		

Residue	F192	R193	M194	F195	D196	V197	G198
GTP	0.00	0.25	0.33	0.68	0.68	0.44	0.10
GDP	0.08	0.34	0.29	0.40	0.46	0.01	0.00
GDI	0.46	0.59	0.30	0.48	0.30	0.35	0.13
Entropy	0.61	0.42	0.81	0.55	0.79	0.70	0.83

Paths from α5 to RasD-HD interface

SSE	β5	LG	αG	L10		α5							
Residue	N265	K266	K267	T320	C321	Q326	N327	V328	K329	F330	V331	F332	D333
GTP	0.11	1.00	0.13	0.34	0.63	0.03	0.96	0.21	0.36	0.40	0.49	0.41	0.50
GDP	0.12	1.00	0.19	0.53	0.46	0.10	0.85	0.23	0.46	0.33	0.31	0.65	0.20
GDI	0.19	1.00	0.06	0.26	0.74	0.08	0.95	0.10	0.18	0.48	0.46	0.48	0.21
Entropy	0.78	0.94	0.14	0.60	0.31	0.25	0.35	0.64	0.25	0.11	0.52	0.56	0.18

SSE	α5					
Residue	A334	V335	T336	D337	I338	I339
GTP	0.36	0.19	0.37	0.38	0.79	1.00
GDP	0.06	0.50	0.65	0.18	0.56	1.00
GDI	0.24	0.39	0.52	0.14	0.24	1.00
Entropy	0.18	0.69	0.24	0.49	0.34	0.74

[a]SSE, secondary structure element.
[b]Entropy, sequence conservation (similar to the definition in (1)) derived from PFAM (2) "seed" alignment with accession number PF00503. Entries≥0.7 are designated as highly conserved and are highlighted in yellow.

Supplemental References

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2. Finn, R. D., Bateman, A., Clements, J., Coggill, P., Eberhardt, R. Y., Eddy, S. R., Heger, A., Hetherington, K., Holm, L., Mistry, J., Sonnhammer, E. L. L., Tate, J., and Punta, M. (2014) Pfam: The protein families database. *Nucleic Acids Res* **42**, D222-D230