

## Supplemental Information

### Automated Prediction

### of Protein Association Rate Constants

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#### Inventory of Supplemental Information

Table S1: data used to draw Figure 2.

Table S2: data used to draw Figure 4.

Figure S1: drawing the same data in Figure 4 in a different way.

**Note:** If Table S2 were a figure, we would group that and Figure S1 as two panels of one supplementary figure. Unfortunately we can't group a table (Table S2) and a figure (Figure S1).

**Table S1. Experimental and predicted  $k_a$  of 45 complexes, related to Figure 2.**

ID	PDB	Proteins	$I$ (M)	Expt $k_a$ ( $M^{-1}s^{-1}$ )	$k_{a0}$ ( $M^{-1}s^{-1}$ )	$\Delta G_{el}^*$ (kcal/mol)	$k_a$ ( $M^{-1}s^{-1}$ )
1	1EQY (A:S)	actin / gelsolin <sup>1</sup>	0.110	2.5E+04	1.1E+06	0.9	2.4E+05
2	2J0T (A:D)	MMP1 / TIMP-1 <sup>2</sup>	0.230	5.2E+04	8.8E+04	0.0	8.9E+04
3	1JWH (CD:A)	casein kinase II $\beta$ chain / $\alpha$ chain <sup>3</sup>	0.160	6.7E+04	3.9E+05	-0.6	1.1E+06
4	2AJF (A:E)	ACE2 receptor / SARS spike protein <sup>4</sup>	0.160	7.1E+04	7.4E+05	-0.1	9.3E+05
5	1KAC (A <sub>3</sub> :B)	Ad12 / coxsackie and adenovirus receptor <sup>5</sup>	0.160	7.3E+04	3.6E+04	-1.1	2.4E+05
6	2I25 (N:L)	shark IgNAR / lysozyme <sup>6</sup>	0.160	9.0E+04	4.5E+05	0.1	3.8E+05
7	1SBB (A:B)	CR2 / Staphylococcus enterotoxin B <sup>7</sup>	0.160	1.0E+05	1.2E+06	0.6	4.8E+05
8	1T6B (X:Y)	anthrax protective antigen / CMG2 <sup>8</sup>	0.050	1.1E+05	1.1E+05	0.8	2.6E+04
9	2VIR (AB:C)	Fab / flu virus hemagglutinin <sup>9</sup>	0.160	1.1E+05	7.7E+05	-0.1	9.4E+05
10	1KKL (ABC:H)	HPrK/P / HPr <sup>10</sup>	0.020	1.3E+05	8.4E+05	1.3	1.0E+05
11	1MQ8 (A:B)	ICAM-1 / integrin $\alpha$ L I domain <sup>11</sup>	0.160	1.3E+05	1.3E+05	0.0	1.4E+05
12	1AKJ (AB:DE)	MHC class 1 HLA-A2 / CD8 <sup>12</sup>	0.160	1.4E+05	2.7E+05	-1.2	2.0E+06
13	1GXD (A:C)	proMMP2 / TIMP-2 <sup>13</sup>	0.166	1.4E+05	2.0E+05	0.0	1.9E+05
14	1UEA (B:A)	TIMP-1 / MMP3 <sup>2</sup>	0.230	2.0E+05	6.1E+04	0.1	5.6E+04
15	1JTG (A:B)	TEM1 / BLIP-II <sup>14</sup>	0.025	2.2E+05	3.7E+05	0.6	1.3E+05
16	1KXQ (H:A)	camel VHH / pancreatic $\alpha$ -amylase <sup>15</sup>	0.206	2.4E+05	2.5E+05	0.3	1.4E+05
17	1E6J (HL:P)	Fab / HIV-1 capsid protein p24 <sup>16</sup>	0.160	3.5E+05	7.4E+05	-0.5	1.8E+06
18	2B42 (B:A)	xylanase / inhibitor <sup>17</sup>	0.100	3.6E+05	4.4E+04	0.1	4.0E+04
19	1QA9 (A:B)	CD2 / CD58 <sup>18</sup>	0.166	4.0E+05	1.2E+05	-1.4	1.2E+06
20	1A22 (A:B)	human growth hormone / hGHbp <sup>19</sup>	0.050	4.0E+05	1.7E+05	-0.5	4.0E+05
21	1E4K (AB:C)	IgG1 Fc / Fc $\gamma$ RIII <sup>20</sup>	0.160	4.2E+05	4.1E+05	-0.3	7.3E+05
22	2B4J (AB:C)	HIV-1 integrase / p75 <sup>21</sup>	0.181	4.8E+05	4.1E+04	-0.5	9.7E+04
23	2VDB (A:B)	albumin / albumin-binding protein <sup>22</sup>	0.160	5.5E+05	1.3E+06	1.2	1.5E+05
24	1KTZ (A:B)	TGF $\beta$ / TGF $\beta$ receptor <sup>23</sup>	0.160	7.4E+05	1.2E+05	-2.3	5.6E+06
25	1GL1 (A:I)	$\alpha$ -chymotrypsin / LCMI II <sup>24</sup>	0.110	8.0E+05	2.6E+05	0.7	7.4E+04
26	1N8O (ABC:E)	chymotrypsin / ecotin <sup>25</sup>	0.210	8.9E+05	1.7E+06	1.1	2.6E+05
27	1JPS (HL:T)	Fab D3H44 / tissue factor <sup>26</sup>	0.160	9.8E+05	2.8E+05	-2.5	1.8E+07
28	3BP8 (AB:C)	Mlc transcription regulator / EIICB <sup>27</sup>	0.223	1.0E+06	7.8E+05	-1.2	6.3E+06
29	1SGN (E:I)	streptogrisin B / OMTKY3 <sup>28</sup>	0.260	1.2E+06	2.3E+05	0.1	1.9E+05
30	1VFB (AB:C)	Fv D1.3 / HEW lysozyme <sup>29</sup>	0.150	1.4E+06	3.2E+05	0.7	1.0E+05
31	1AGR (A:E)	G $\alpha_{i1}$ / RGS4 <sup>30</sup>	0.110	1.7E+06	2.7E+04	-3.1	5.0E+06
32	1FLE (E:I)	elastase / elafin <sup>31</sup>	0.250	3.6E+06	2.9E+06	0.3	1.7E+06
33	2BTF (A:P)	$\beta$ actin / profilin <sup>32</sup>	0.025	6.6E+06	3.6E+05	-2.5	2.4E+07
34	1LFD (B:A)	Ras / RalGDS <sup>33</sup>	0.030	7.7E+06	2.0E+05	-2.8	2.2E+07
35	1OC0 (A:B)	plasminogen activator inhibitor-1 / SMB <sup>34</sup>	0.165	1.4E+07	1.9E+05	-1.0	1.0E+06
36	1MAH (A:F)	AchE / fasciculin-II <sup>35</sup>	0.100	1.5E+07	2.3E+05	-2.5	1.7E+07
37	1EWY (A:C)	ferredoxin reductase / ferredoxin <sup>36</sup>	0.310	4.0E+07	1.0E+05	-1.5	1.4E+06
38	1BML (C:A)	streptokinase / plasmin <sup>37</sup>	0.100	5.4E+07	9.3E+04	-4.1	8.4E+07

39	1FFW (A:B)	CheY / CheA <sup>38</sup>	0.150	6.2E+07	3.8E+05	-1.9	9.0E+06
40	4HTC (HL:I)	thrombin / hirudin <sup>39</sup>	0.175	7.5E+07	4.0E+05	-3.4	1.3E+08
41	1EMV (B:A)	Colicin E9 / Im9 <sup>40</sup>	0.250	9.0E+07	4.8E+05	-2.2	2.1E+07
42	1I2M (A:B)	Ran GTPase / RCC1 <sup>41</sup>	0.045	1.0E+08	1.1E+05	-7.0	1.1E+09
43	1BRS (A:D)	barnase / barstar <sup>42</sup>	0.103	1.2E+08	9.2E+04	-3.2	1.9E+07
44	1UDI (E:I)	uracil-DNA glycosylase / inhibitor <sup>43</sup>	0.080	1.5E+08	8.1E+05	-3.9	5.8E+08
45	2PCF (B:A)	cytochrome <i>f</i> / plastocyanin <sup>44</sup>	0.100	1.8E+08	6.0E+05	-4.4	8.4E+08
46	1DFJ (E:I)	ribonuclease A / inhibitor <sup>45</sup>	0.200	3.4E+08	6.6E+05	-2.5	4.2E+07
47	1E6E (A:B)	adrenoxin reductase / adrenoxin <sup>46</sup>	0.210	4.0E+08	3.0E+05	-3.8	1.8E+08
48	7CEI (A:B)	Colicin E7 nuclease / Im7 <sup>47</sup>	0.250	7.6E+08	2.1E+05	-5.8	1.3E+09
49	2PCC (A:B)	cytochrome c peroxidase / cytochrome c <sup>48</sup>	0.150	1.3E+09	4.5E+05	-7.2	4.3E+09

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**Table S2. Predicted  $k_a$  of 132 complexes, related to Figure 4.**

<b>PDB</b>	$k_{a0}$ ( $M^{-1}s^{-1}$ )	$\Delta G_{el}^*$ (kcal/mol)	$k_a$ ( $M^{-1}s^{-1}$ )
Rigid-body category			
1AHW (AB:C)	2.7E+05	-2.2	1.0E+07
1AK4 (A:D)	1.5E+06	-0.2	2.1E+06
1AKJ (AB:DE)	2.7E+05	-1.2	2.2E+06
1AVX (A:B)	6.0E+03	-1.3	5.2E+04
1AY7 (A:B)	7.9E+04	-0.8	3.0E+05
1AZS (AB:C)	1.4E+05	-0.7	4.8E+05
1B6C (A:B)	1.5E+05	0.5	6.0E+04
1BUH (A:B)	9.1E+05	-0.1	1.1E+06
1BVN (P:T)	9.7E+04	0.6	3.8E+04
1CLV (A:I)	2.8E+05	0.9	5.8E+04
1D6R (A:I)	3.0E+03	-0.1	3.8E+03
1DFJ (E:I)	6.6E+05	-2.9	9.5E+07
1DQJ (AB:C)	3.9E+05	1.0	7.5E+04
1E6E (A:B)	3.0E+05	-4.4	4.4E+08
1E6J (HL:P)	7.4E+05	-0.6	1.9E+06
1E96 (A:B)	2.9E+04	-0.9	1.3E+05
1EFN (B:A)	6.7E+05	-0.6	1.8E+06
1EWY (A:C)	1.0E+05	-2.6	7.6E+06
1F34 (A:B)	1.1E+06	2.3	2.2E+04
1F51 (AB:E)	1.8E+05	0.9	4.1E+04
1FC2 (C:D)	5.9E+05	0.5	2.5E+05
1FCC (AB:C)	2.1E+05	0.7	6.9E+04
1FFW (A:B)	3.8E+05	-1.9	9.1E+06
1FLE (E:I)	2.9E+06	0.3	1.8E+06
1FQJ (A:B)	1.3E+05	-2.3	6.0E+06
1FSK (BC:A)	7.8E+04	0.7	2.3E+04
1GL1 (A:I)	2.6E+05	0.7	8.0E+04
1GLA (G:F)	4.0E+04	-2.7	3.9E+06
1GPW (A:B)	3.8E+05	-4.8	9.5E+08
1GXD (A:C)	2.0E+05	0.0	2.1E+05
1H9D (A:B)	1.6E+05	0.4	8.1E+04
1HE1 (C:A)	9.8E+04	-0.1	1.2E+05
1HIA (AB:I)	2.1E+05	-1.3	2.0E+06
1I4D (D:AB)	8.4E+04	0.5	3.8E+04
1I9R (HL:ABC)	7.4E+05	-0.7	2.5E+06
1J2J (A:B)	3.9E+05	-0.3	6.5E+05
1JPS (HL:T)	2.8E+05	-2.5	1.9E+07
1JTG (A:B)	3.7E+05	0.3	2.3E+05
1JWH (CD:A)	3.9E+05	-0.7	1.2E+06
1K4C (AB:C)	4.1E+05	-1.6	5.7E+06
1K74 (AB:DE)	7.2E+05	-1.7	1.3E+07
1KAC (A <sub>3</sub> :B)	3.6E+04	-1.1	2.5E+05
1KLU (AB:D)	5.5E+05	-0.6	1.4E+06
1KTZ (A:B)	1.2E+05	-2.3	5.9E+06
1KXQ (H:A)	2.5E+05	0.2	1.8E+05
1MAH (A:F)	2.3E+05	-2.1	7.6E+06
1ML0 (AB:D)	2.6E+05	-4.9	7.6E+08
1MLC (AB:E)	2.6E+05	-0.5	5.8E+05
1N8O (ABC:E)	1.7E+06	1.1	2.4E+05
1NCA (HL:N)	3.3E+05	-0.3	5.4E+05

1NSN (HL:S)	5.4E+04	1.0	1.1E+04
1OC0 (A:B)	1.9E+05	-1.0	1.1E+06
1OFU (A:XY)	3.0E+05	-0.2	4.1E+05
1OYV (A:I)	1.7E+06	0.6	6.5E+05
1OYV (B:I)	2.6E+05	1.4	2.5E+04
1PVH (A:B)	2.9E+05	0.1	2.4E+05
1QA9 (A:B)	1.2E+05	-1.4	1.3E+06
1QFW (HL:AB)	1.8E+05	-0.5	4.2E+05
1QFW (IM:AB)	3.2E+05	-0.6	9.0E+05
1RLB (ABCD:E)	9.0E+05	0.3	5.7E+05
1RV6 (VW:X)	4.3E+05	0.3	2.7E+05
1S1Q (A:B)	1.6E+05	-0.1	2.0E+05
1SBB (A:B)	1.2E+06	0.6	4.8E+05
1SGN (E:I)	2.3E+05	0.0	2.2E+05
1T6B (X:Y)	1.1E+05	1.2	1.3E+04
1UDI (E:I)	8.1E+05	-2.9	1.1E+08
1US7 (A:B)	1.8E+05	-0.6	4.7E+05
1VFB (AB:C)	3.2E+05	0.7	1.0E+05
1WEJ (HL:F)	3.6E+05	-2.5	2.6E+07
1YVB (A:I)	1.4E+05	-0.6	3.4E+05
1Z0K (A:B)	8.3E+05	-0.3	1.4E+06
1ZHI (A:B)	2.1E+05	-1.6	3.4E+06
2A5T (A:B)	1.4E+05	-0.3	2.2E+05
2A9K (A:B)	1.8E+05	-1.2	1.3E+06
2ABZ (B:E)	4.0E+06	0.6	1.3E+06
2AJF (A:E)	7.4E+05	-0.1	9.5E+05
2B42 (B:A)	4.4E+04	0.1	3.9E+04
2B4J (AB:C)	4.1E+04	-0.5	1.0E+05
2BTF (A:P)	3.6E+05	-1.9	8.4E+06
2FD6 (HL:U)	7.9E+05	-1.1	5.0E+06
2FJU (A:B)	2.6E+05	-0.3	4.3E+05
2G77 (A:B)	1.3E+05	-0.7	3.8E+05
2HLE (A:B)	3.8E+05	-0.4	7.2E+05
2I25 (N:L)	4.5E+05	0.1	3.8E+05
2J0T (A:D)	8.8E+04	-0.2	1.2E+05
2JEL (HL:P)	2.2E+05	0.2	1.5E+05
2MTA (HL:A)	3.4E+05	-0.4	6.1E+05
2O8V (A:B)	2.8E+05	-0.1	3.4E+05
2OOB (A:B)	2.7E+06	-0.1	3.1E+06
2OOR (AB:C)	9.5E+04	-1.9	2.3E+06
2OUL (A:B)	1.3E+06	-0.2	1.7E+06
2PCC (A:B)	4.5E+05	-7.2	4.2E+09
2VDB (A:B)	1.3E+06	1.2	1.5E+05
2VIR (AB:C)	7.7E+05	-0.1	9.6E+05
3BP8 (AB:C)	7.8E+05	-1.4	8.6E+06
3D5S (A:C)	2.1E+05	-1.8	4.5E+06
3OED (A:B)	3.4E+05	-4.0	2.6E+08
7CEI (A:B)	2.1E+05	-7.0	1.9E+09
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Medium-difficulty category			
1GP2 (A:BG)	6.1E+05	-0.4	1.3E+06
1HE8 (A:B)	2.4E+05	-1.7	4.0E+06
1I2M (A:B)	1.1E+05	-4.3	1.3E+08
1IJK (A:BC)	3.7E+05	-5.4	1.8E+09
1K5D (AB:C)	4.5E+05	-2.1	1.7E+07
1KKL (ABC:H)	8.4E+05	0.7	2.6E+05

1LFD (B:A)	2.0E+05	-2.5	1.5E+07
1M10 (A:B)	1.9E+06	-3.0	3.0E+08
1MQ8 (A:B)	1.3E+05	0.0	1.4E+05
1NW9 (B:A)	2.1E+05	0.9	4.6E+04
1R6Q (A:C)	3.3E+05	0.5	1.5E+05
1XQS (A:C)	5.9E+05	-2.6	4.4E+07
2CFH (A:C)	2.8E+05	1.2	3.5E+04
2H7V (C:A)	2.7E+05	0.6	9.6E+04
2HRK (A:B)	1.8E+05	0.0	1.9E+05
2J7P (A:D)	5.4E+04	-0.9	2.6E+05
2NZ8 (A:B)	5.5E+05	0.2	4.0E+05
3CPH (A:G)	2.6E+05	-1.5	3.4E+06
4CPA (A:I)	9.5E+05	0.9	1.9E+05
Difficult category			
1ATN (A:D)	3.5E+05	-0.2	5.0E+05
1DE4 (AB:CF)	2.2E+05	-0.5	5.0E+05
1E4K (AB:C)	4.1E+05	-0.4	7.6E+05
1F6M (A:C)	5.1E+05	0.5	2.0E+05
1FQ1 (A:B)	7.4E+05	-0.3	1.3E+06
1H1V (A:G)	5.7E+05	0.8	1.6E+05
1JZD (AB:C)	7.0E+05	1.4	6.3E+04
1Y64 (B:A)	1.7E+05	0.5	7.7E+04
1ZLI (A:B)	5.0E+05	2.2	1.3E+04
1ZM4 (A:B)	7.3E+05	2.6	8.9E+03
2COL (A:B)	8.3E+04	2.1	2.6E+03
2HMI (AB:CD)	2.7E+05	2.3	5.5E+03
2IDO (A:D)	8.1E+04	-0.5	2.0E+05
2O3B (A:B)	2.4E+05	-2.4	1.5E+07
2OT3 (A:B)	4.0E+05	-0.9	1.9E+06

All  $\Delta G_{el}^*$  calculations were done at ionic strength = 0.15 M.

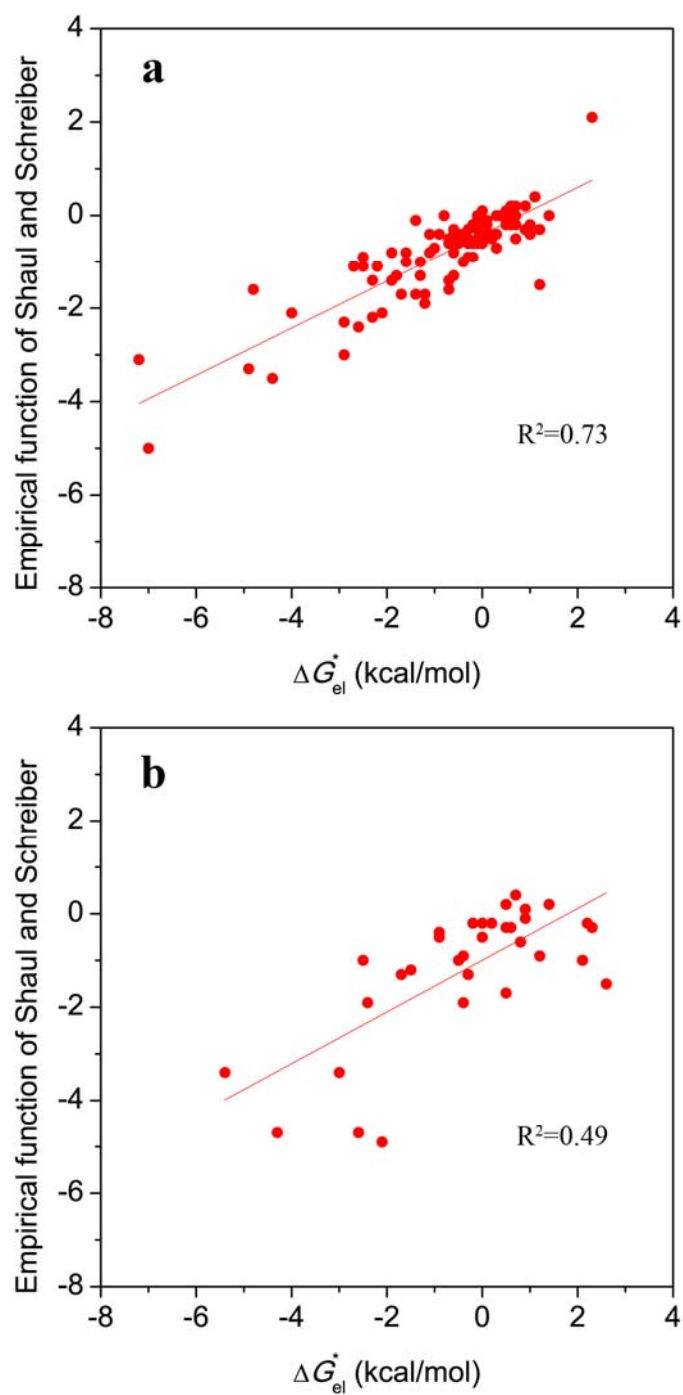


Figure S1. Correlation of the empirical function of Shaul and Schreiber (2005) with  $\Delta G_{el}^{\ddagger}$ . (a) The 98 cases in the rigid-body category. (b) The 34 cases in the medium-difficulty and difficult categories. The correlation  $R^2$  values are shown in the figure. The values of  $\Delta G_{el}^{\ddagger}$  are those listed in [Table S2](#).