**Supplementary File 1**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **#NLSs** | **A** | **Astdev** | **IMAX1** | **IMAX1, stdev** | **τ1** | **τ1,stdev** | **IMAX2** | **IMAX2, stdev** | **τ2** | **Τ2,stdev** |
| **MS2S37P** | 0 | 0.19 | 0.01 | 0.13 | 0.01 | 0.13 | 0.03 | 0.68 | 0.26 | 0.006 | 0.00 |
| 14 | 0.64 | 0.04 | -0.03 | 15.16 | 0.08 | 8.72 | 0.97 | 15.15 | 0.055 | 0.17 |
| 19 | 0.87 | 0.14 | 8.92 | 8.44 | 0.06 | 0.02 | 6.50 | 18.07 | 0.01 | 0.04 |
| 23 | 0.52 | 0.22 | 12.71 | 1.50E+04 | 0.06 | 2.31 | 4.24 | 1.50E+04 | 0.04 | 5.80 |
| 29 | 0.40 | 0.28 | 27.77 | 3.77E+02 | 0.02 | 0.09 | 6.00 | 3.87E+02 | 0.04 | 0.35 |
| 38 | 0.88 | 0.59 | 28.72 | 2.55E+03 | 0.05 | 0.14 | 19.64 | 2.55E+03 | 0.02 | 0.37 |
| 54 | 2.04 | 0.39 | 34.09 | 9.21E+03 | 0.03 | 0.26 | 20.79 | 9.23E+03 | 0.03 | 0.62 |
| **I53-47** | 0 | 0.16 | 0.02 | 0.27 | 0.36 | 0.06 | 0.06 | 3.52 | 4.55 | 0.00 | 0.01 |
| 15 | 0.53 | 0.12 | 2.75 | 0.20 | 0.14 | 0.02 | 3.71 | 1.09 | 0.01 | 0.01 |
| 18 | 3.09 | 0.07 | 1.98 | 0.67 | 0.07 | 0.02 | 9.57 | 25.84 | 0.00 | 0.01 |
| 22 | 0.00 | 3.44 | 9.68 | 112.66 | 0.05 | 3.6E-01 | -0.10 | 3.99E+06 | 0.00 | 3.52E+03 |
| 22 | 1.88 | 0.23 | 5.29 | 9.68 | 0.04 | 0.05 | 0.60 | 3.18E+03 | 0.00 | 4.28 |
| 25 | 2.24 | 0.14 | 2.84 | 2.03 | 0.06 | 0.03 | 0.85 | 7.71E+02 | 0.00 | 0.83 |
| 30 | 1.75 | 0.20 | 2.35 | 0.36 | 0.19 | 0.05 | 6.38 | 0.36 | 0.04 | 0.00 |
| 35 | 1.23 | 0.29 | 6.70 | 51.21 | 0.03 | 0.11 | 11.25 | 53.48 | 0.05 | 0.08 |
| 37 | 0.99 | 0.20 | 3.00 | 2.36E+03 | 0.07 | 3.06 | 3.43 | 2.36E+03 | 0.06 | 2.44 |
| 37 | 2.15 | 0.36 | 3.19 | 7.92 | 0.11 | 0.13 | 11.37 | 7.84 | 0.04 | 0.02 |
| 41 | 1.07 | 0.23 | 4.90 | 7.68 | 0.01 | 0.04 | 11.97 | 4.51 | 0.06 | 0.02 |
| 44 | 0.00 | 0.23 | 9.05 | 5.12E+05 | 0.05 | 34.56 | 1.93 | 5.12E+05 | 0.05 | 162.87 |
| **MS2** | 0 | 0.07 | 0.00 | 0.09 | 0.03 | 0.07 | 0.02 | 1.47 | 7.42 | 0.00 | 0.01 |
| 42 | 0.32 | 0.06 | 0.41 | 0.05 | 0.33 | 0.07 | 0.35 | 0.02 | 0.04 | 0.01 |
| 54 | 0.10 | 0.07 | 1.04 | 0.07 | 0.30 | 0.04 | 0.15 | 0.08 | 0.06 | 0.03 |
| 57 | 0.06 | 0.03 | 0.23 | 1.17E+03 | 0.07 | 13.60 | 1.60 | 1.17E+03 | 0.08 | 2.07 |
| 77 | 0.48 | 0.04 | 0.92 | 2.74E+03 | 0.07 | 1.77 | 0.42 | 2.74E+03 | 0.07 | 3.92 |
| 86 | 0.52 | 0.04 | 1.95 | 3.43 | 0.05 | 0.04 | 0.86 | 2.75 | 0.02 | 0.08 |
| 93 | 0.37 | 0.03 | 1.76 | 0.53 | 0.06 | 0.01 | 1.63 | 13.32 | 0.00 | 0.04 |
| 98 | 0.21 | 0.04 | 1.79 | 2.84E+03 | 0.04 | 0.47 | 1.77 | 2.84E+03 | 0.04 | 0.45 |

Notably, although bi-exponential fits provided marginally better fit quality, it was at the expense of very high error bars on the parameter estimates, indicative of over-fitting and “sloppiness” (Gutenkunst, Ryan N., et al. "Universally sloppy parameter sensitivities in systems biology models." *PLoS computational biology* 3.10 (2007)). This is evident in the standard deviation (stdev) recovered from fit for every parameter in the table. Moreover, we observe that despite the large errors on the fitting parameters in the bi-exponential fit, the combinations of these parameters that correspond to parameters in the mono-exponential fit are tightly constrained to values of the mono-exponential fit parameters. Namely, and , as shown in the table below.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **#NLSs** | **IMAX (mono-exponential)** | **IMAX1 + IMAX2**  **(bi-exponential)** | **IMAX\* τ (mono-exponential)** | **IMAX1\*τ1 + IMAX2\*τ2**  **(bi-exponential)** |
| **MS2S37P** | 0 | 0.39 | 0.81 | 0.01 | 0.02 |
| 14 | 0.94 | 0.94 | 0.05 | 0.05 |
| 19 | 12.44 | 15.42 | 0.51 | 0.59 |
| 23 | 16.63 | 16.95 | 0.88 | 0.90 |
| 23 | 32.88 | 33.77 | 0.74 | 0.77 |
| 38 | 43.59 | 48.36 | 1.62 | 1.84 |
| 54 | 49.76 | 54.88 | 1.43 | 1.64 |
| **I53-47** | 0 | 2.04 | 3.79 | 0.02 | 0.03 |
| 15 | 3.83 | 6.47 | 0.18 | 0.43 |
| 18 | 4.22 | 11.55 | 0.17 | 0.17 |
| 22 | 3.01 | 9.59 | 0.16 | 0.45 |
| 22 | 5.35 | 5.89 | 0.21 | 0.22 |
| 25 | 2.86 | 3.70 | 0.19 | 0.17 |
| 30 | 7.57 | 8.73 | 0.37 | 0.69 |
| 35 | 17.39 | 17.95 | 0.75 | 0.80 |
| 37 | 6.45 | 6.43 | 0.41 | 0.41 |
| 37 | 14.01 | 14.56 | 0.73 | 0.84 |
| 41 | 14.12 | 16.87 | 0.72 | 0.81 |
| 44 | 11.01 | 10.98 | 0.51 | 0.52 |
| **MS2** | 0 | 0.25 | 1.56 | 0.00 | 0.01 |
| 42 | 0.50 | 0.76 | 0.03 | 0.15 |
| 54 | 1.04 | 1.19 | 0.23 | 0.33 |
| 57 | 1.83 | 1.83 | 0.14 | 0.14 |
| 77 | 1.33 | 1.33 | 0.09 | 0.09 |
| 86 | 2.62 | 2.80 | 0.11 | 0.12 |
| 93 | 2.09 | 3.39 | 0.10 | 0.11 |
| 98 | 3.56 | 3.56 | 0.14 | 0.14 |