**A**

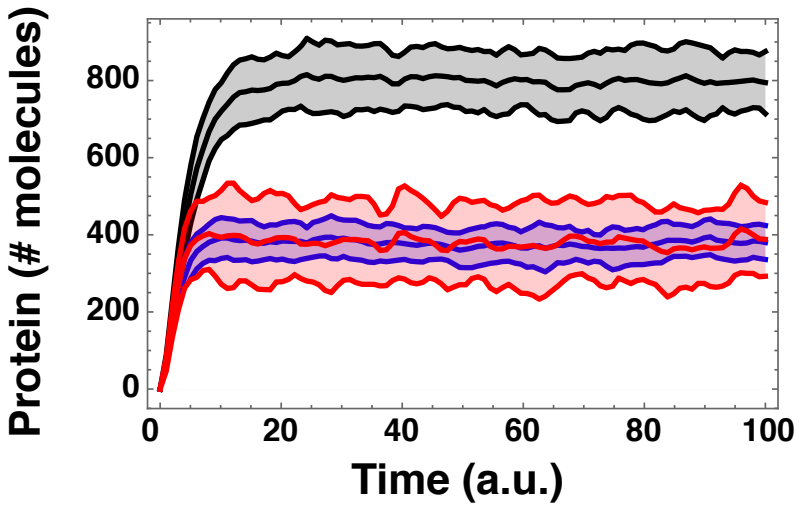
| Model | Burst Freq. | $b_{P_{eff}}$ | $b_{r_{eff}}$ | ITI* | Analytical Prediction <P> | Analytical Prediction Variance | Analytical Prediction Fano factor | Analytical Prediction $CV^2$ | From Simulations <P> | From Simulations Variance | From Simulations Fano factor | From Simulations $CV^2$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Two-state Model (High mean) | 0.091 | 100 | 20 | 0 | 18182 | 36363636 | 2000 | 0.11 | 17466 (±1060) | 33912654 (±3230930) | 1954 (±311) | 0.11 (±0.02) |
| Two-state Model (one-half mean) | 0.046 | 100 | 20 | 0 | 9091 | 18182000 | 2000 | 0.22 | 9614 (±27) | 19601286 (±1077555) | 2039 (±118) | 0.21 (±0.01) |
| Auto-repression (one-half mean) | 0.046 | 100 | 20 | ≤ 1 | 9091 | 9091000 | ≥ 1000 | ≥ 0.11 | 9049 (±89) | 11189103 (±964941) | 1237 (±114) | 0.14 (±0.01) |
| Auto-depletion (one-half mean) | 0.091 | 50 | 20 | ≤ 1 | 9091 | 6060606 | ≥ 500 | ≥ 0.055 | 9336 (±164) | 5716108 (±381944) | 612 (±30) | 0.07 (±0.01) |
| Auto-repression (one-third mean) | 0.030 | 100 | 20 | ≤ 2 | 6061 | 8661169 | ≥ 667 | ≥ 0.11 | 5248 (±219) | 6611475 (±163289) | 1260 (±21) | 0.24 (±0.01) |
| Auto-depletion (one-third mean) | 0.091 | 33.3 | 20 | ≤ 2 | 6061 | 2000130 | ≥ 222 | ≥ 0.037 | 5078 (±13) | 1675023 (±126109) | 330 (±26) | 0.06 (±0.01) |

i i

ii ii

*For the analytical predictions the linear feedback approximation was used where $|T| = \frac{\langle p \rangle_{NFB}}{\langle p \rangle_{FB}} - 1$. The subscript NFB means without feedback and the subscript FB means with feedback. Since the linear feedback approximation does not saturate, it overestimates the magnitude of $|T|$ for realistic repression relationships that do saturate. Accordingly, the analytical predictions for Fano factor and $CV^2$ should be interpreted as lower limits.

**B**




**C**

| | Two State | Two State (lower mean) | Transcriptional Negative FB | Precursor Depletion FB | Simple RNA Depletion FB |
|---|---|---|---|---|---|
| Mean | 800 | 400 | 381 | 376 | 381 |
| $CV_2$ | 0.01 | 0.025 | 0.07 | 0.009 | 0.008 |
| Fano | 8.5 | 9.5 | 30 | 5.6 | 3.2 |

**D**