

Appendix 3

1 Fitting the experimental profiles by MM5 model : Unchallenged S phase

We fitted independently the measured profiles for each global replicated fraction by discrete MM5 model. The fits of observations from 8% global replicated fraction are presented in Appendix 1, Figure 9 and those of 19% and 53% are presented in Figures 1 and 2 respectively. In TABLE 1 we give the value of the fitted parameters. The reliability of observed differences among inferred MM5 parameters are assessed statistically by using χ^2 coefficient as defined in Appendix 2 (Figure 3).

Corrected/S3-Figure1.png

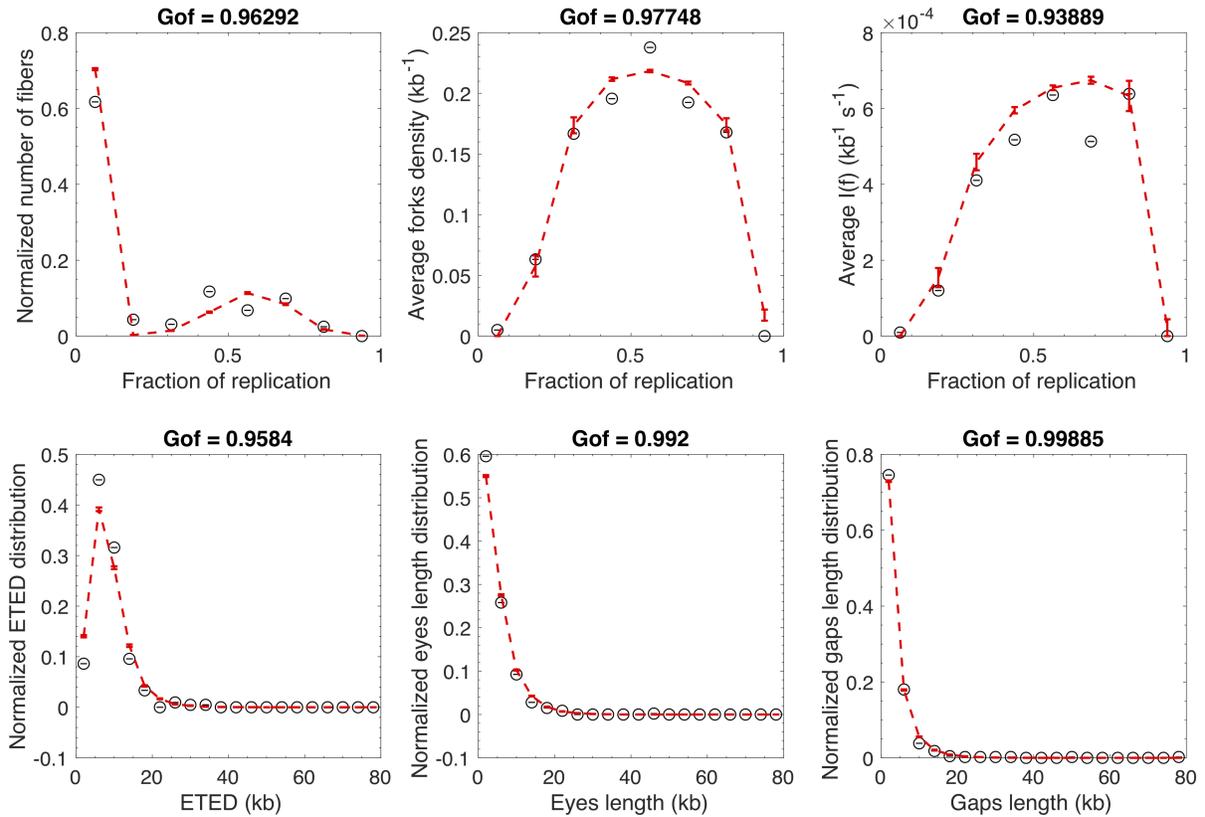


Fig 1. Modeling measured sample with 19% global replicated fraction with the discrete MM5 model. Open circles are simulated data and the red dashed line is the fit. $GoF_{global} = 0.96$

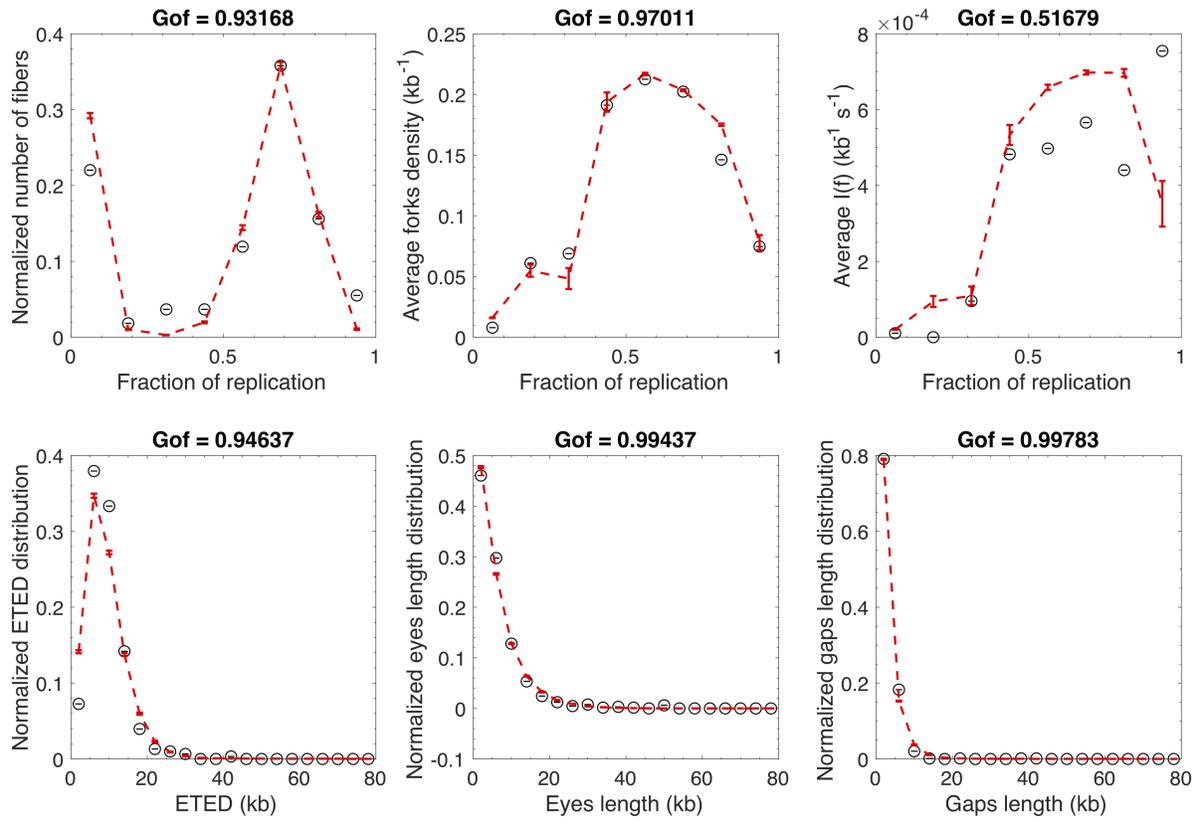


Fig 2. Modeling measured sample with 53% global replicated fraction with the discrete MM5 model. Open circles are simulated data and the red dashed line is the fit. $GoF_{global} = 0.90$

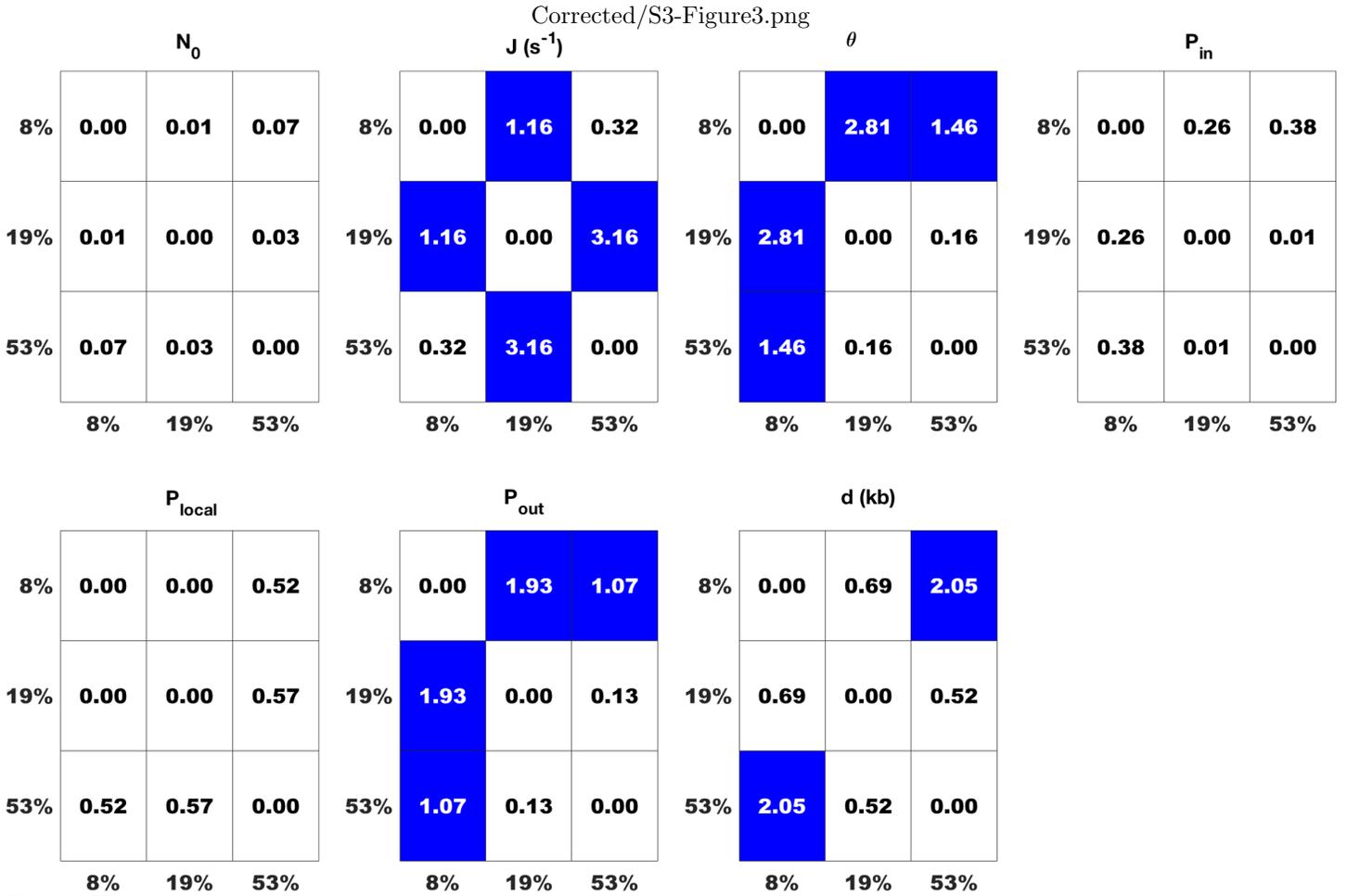


Fig 3. The values of each MM5 model parameter were compared pair-wise between samples with different global replicated fraction. The statistical significance of their difference was assessed by χ^2 test and represented as a binary heat map where the white colour represents no statistically significant difference and the blue colour represents statistically significant difference. The number in each box is the χ^2 coefficient.

2 Fitting the experimental profiles by MM5 model : Chk1 inhibited S phase

We fitted with the discrete MM5 model a sample that had spent in the presence of UCN-01 the same time interval in S phase as the control sample with 8% global replicated fraction. The global replicated fraction of the of the UCN-01 sample was 22%. The fits are presented in Figure 4 and the obtained parameters values are given in TABLE 1. The reliability of observed differences among inferred MM5 parameters between controls and Chk1 inhibited sample are assessed statistically by using χ^2 coefficient as defined in Appendix 2 (Figure 5).

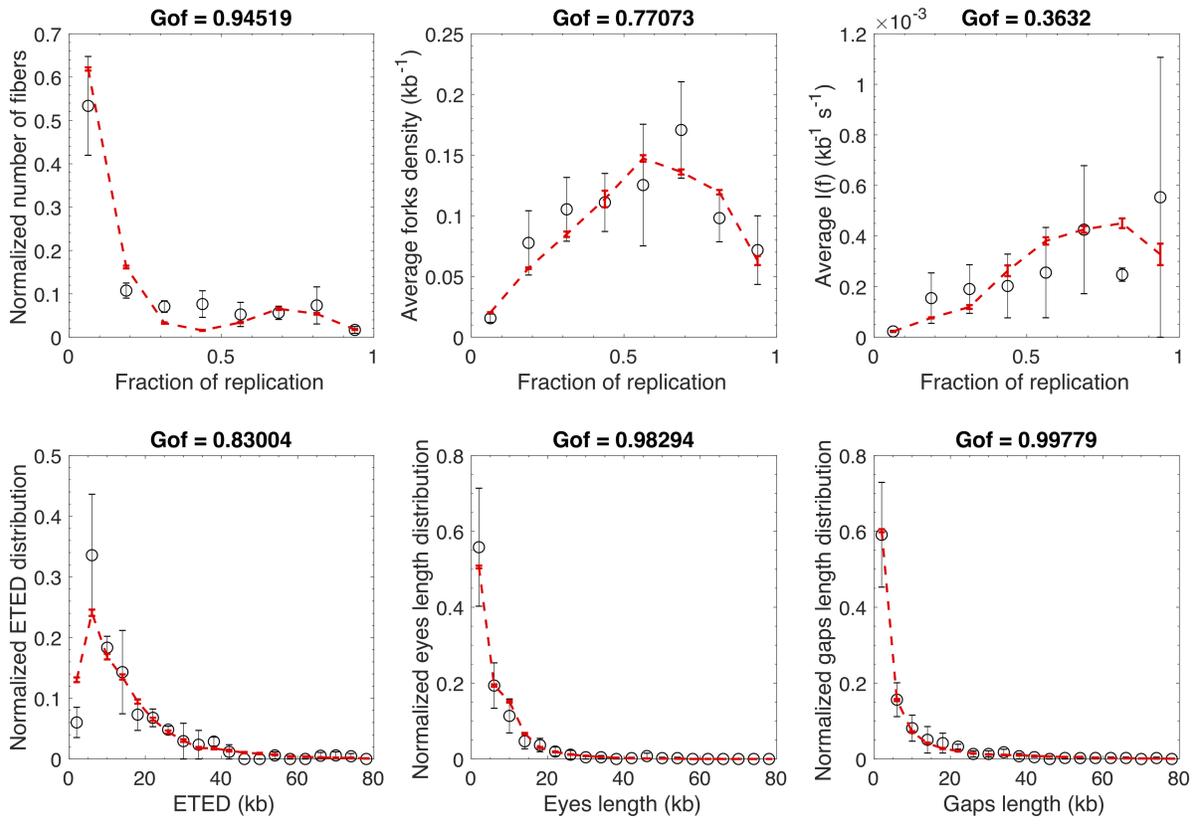


Fig 4. Modeling a measured sample with 22% global replicated fraction in presence of UCN-01 with discrete MM5 model. Open circles are simulated data and the red dashed line is the fit. $Gof_{global} = 0.85$

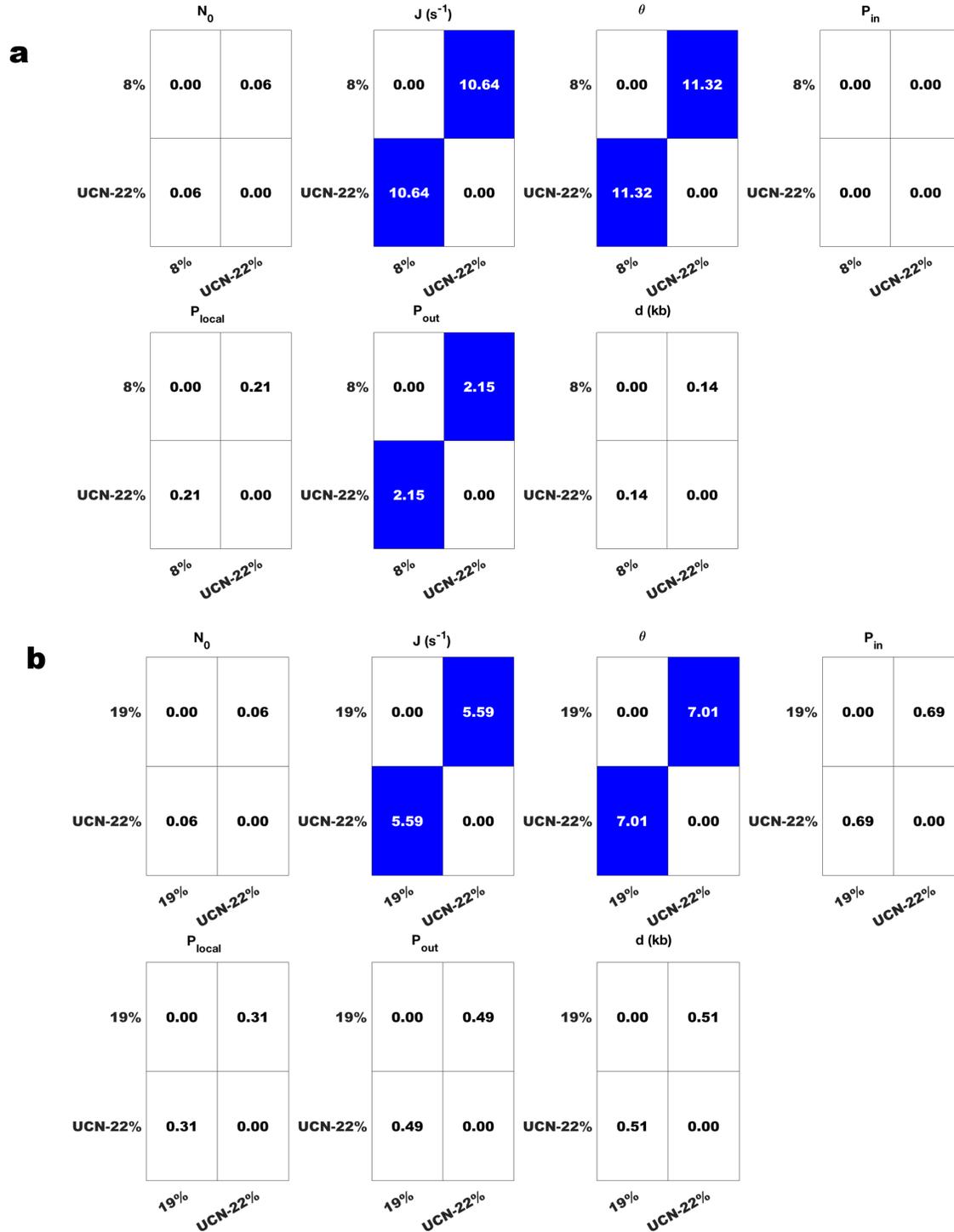


Fig 5. a. Comparing samples that have spent the same time interval in S phase. b. Comparing samples that have similar global replication fractions. The values of each MM5 model parameter were compared pair-wise between samples with different global replicated fraction. The statistical significance of their difference was assessed by χ^2 test and represented as a binary heat map where the white colour represents no statistically significant difference and the blue colour represents statistically significant difference. The number in each box is the χ^2 coefficient.

3 Fitting the experimental profiles by MM5 model : Chk1 over-expressed S phase

We fitted with the discrete MM5 model a Chk1 over-expressed sample with the same incubation time than the control sample with 46% global replicated fraction. The global replicated fraction of the of the Chk1 over-expressed sample was 22%. The fits are presented in Figures 6 and 7 and the obtained parameters values are given in TABLE 1. The reliability of observed differences among inferred MM5 parameters between controls and Chk1 over-expressed sample are assessed statistically by using χ^2 coefficient as defined in Appendix 2 (Figure 8).

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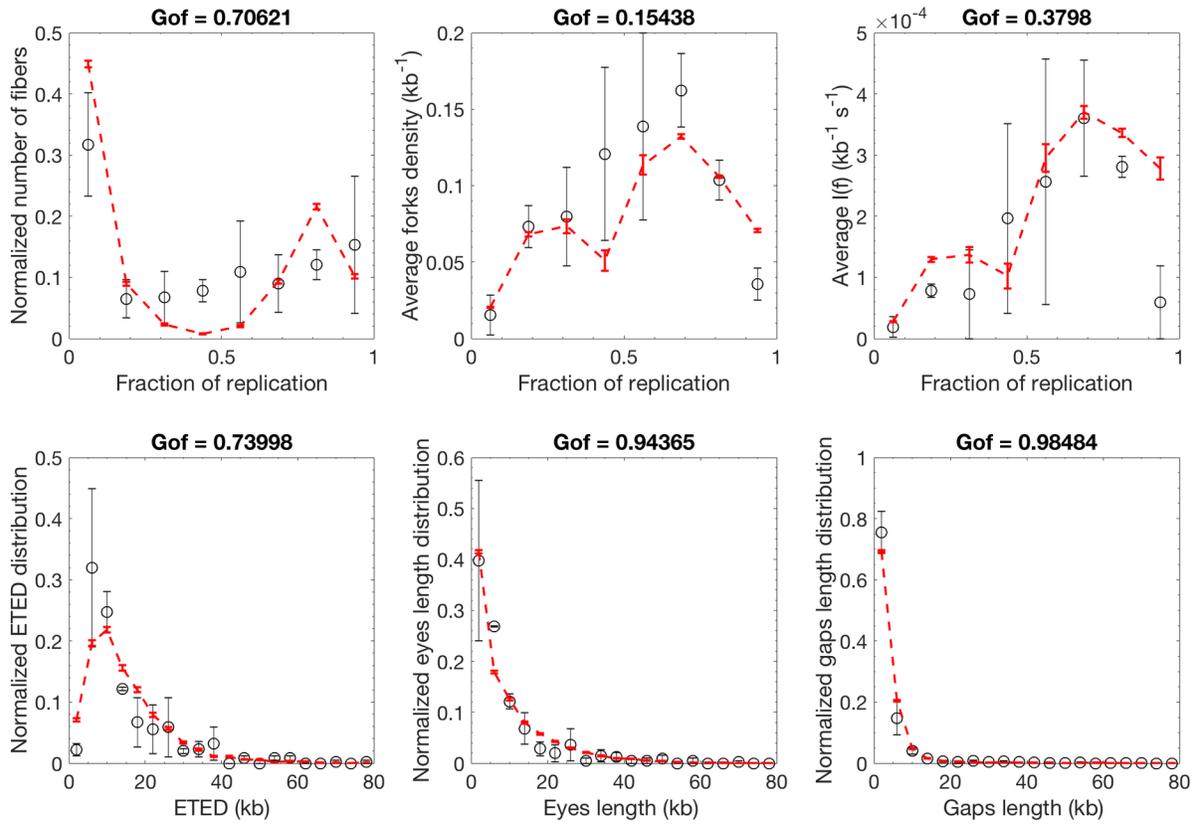


Fig 6. Modeling a measured sample with 46% global replicated fraction with discrete MM5 model. Open circles are simulated data and the red dashed line is the fit. $Gof_{global} = 0.65$

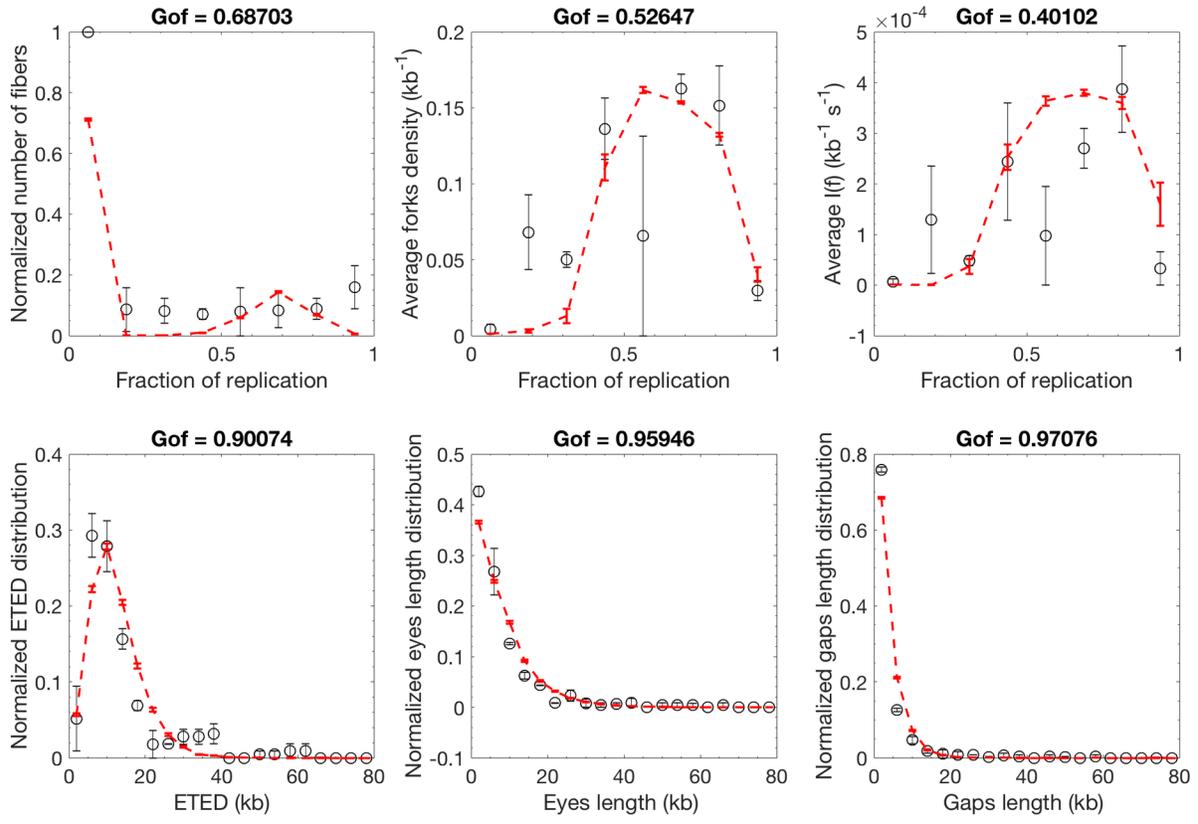


Fig 7. Modeling a measured sample with 22% global replicated fraction where Chk1 is over-expressed with discrete MM5 model. Open circles are simulated data and the red dashed line is the fit. $Gof_{global} = 0.74$

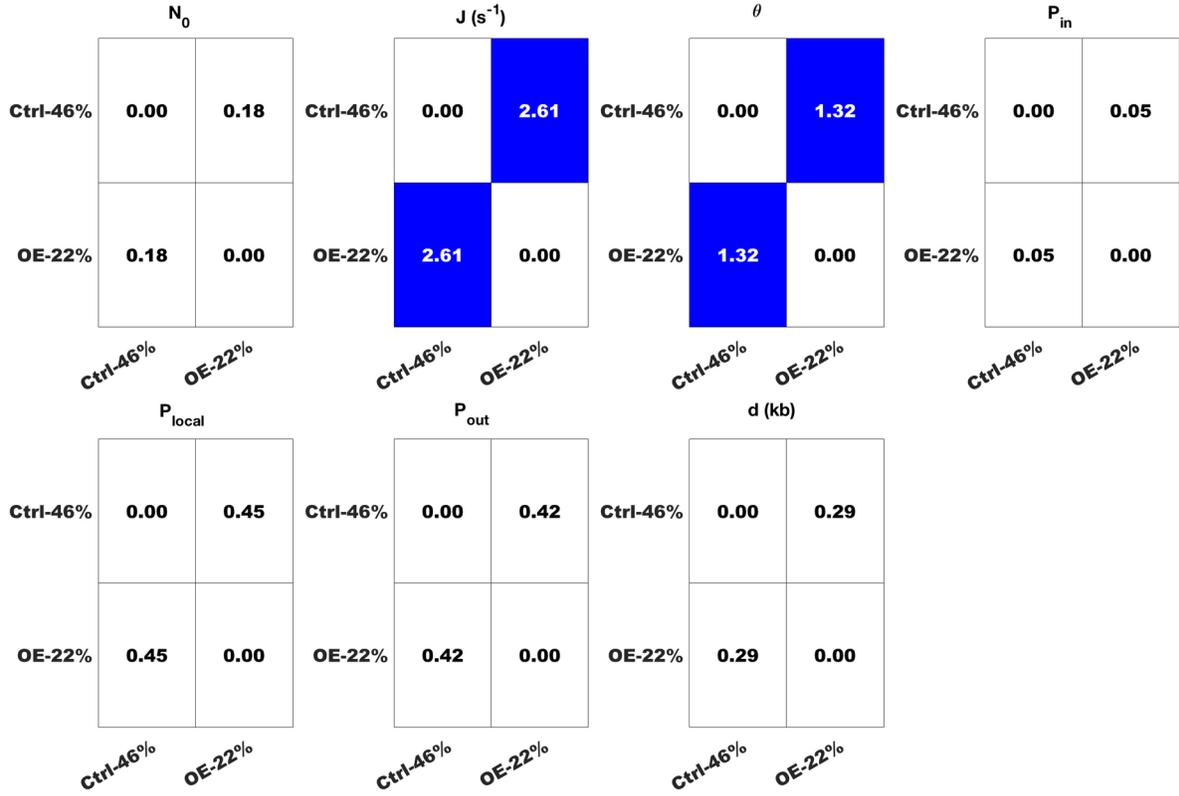


Fig 8. Comparing samples that have spent the same time interval in S phase. The values of each MM5 model parameter were compared pair-wise between samples with different global replicated fraction. The statistical significance of their difference was assessed by χ^2 test and represented as a binary heat map where the white colour represents no statistically significant difference and the blue colour represents statistically significant difference. The number in each box is the χ^2 coefficient.

Table 1. Values and the corresponding errors of MM5 parameters for the best fit of each sample and each condition.

| MM5 | unchallenged: 8% | unchallenged: 19% | unchallenged: 53% | UCN-01: 22% | unchallenged: 46% | over-expressed: 22% |
|--------------|------------------|-------------------|-------------------|------------------|-------------------|---------------------|
| N_0 | 1064 ± 135 | 1043 ± 116 | 1002 ± 106 | 1006 ± 102 | 880 ± 58.5 | 784 ± 58.7 |
| $J (s^{-1})$ | 601 ± 198 | 1026 ± 196 | 404 ± 151 | 1467 ± 89 | 1190 ± 114 | 569 ± 82.1 |
| θ | 0.25 ± 0.06 | 0.43 ± 0.04 | 0.39 ± 0.05 | 0.56 ± 0.032 | 0.50 ± 0.01 | 0.42 ± 0.02 |
| P_{in} | 0.41 ± 0.07 | 0.34 ± 0.07 | 0.32 ± 0.07 | 0.42 ± 0.07 | 0.33 ± 0.03 | 0.36 ± 0.04 |
| P_{local} | 0.43 ± 0.06 | 0.43 ± 0.06 | 0.52 ± 0.06 | 0.38 ± 0.06 | 0.37 ± 0.03 | 0.45 ± 0.03 |
| P_{out} | 0.09 ± 0.02 | 0.17 ± 0.04 | 0.15 ± 0.03 | 0.23 ± 0.04 | 0.15 ± 0.02 | 0.23 ± 0.03 |
| $d (kb)$ | 143.8 ± 36.3 | 91.5 ± 25.6 | 56.1 ± 23.6 | 119.3 ± 29.3 | 139.9 ± 16.9 | 178.4 ± 18.7 |

References