Interdivision time correlations on **lineage trees** reveal **underlying biological oscillators** driving the cell cycle

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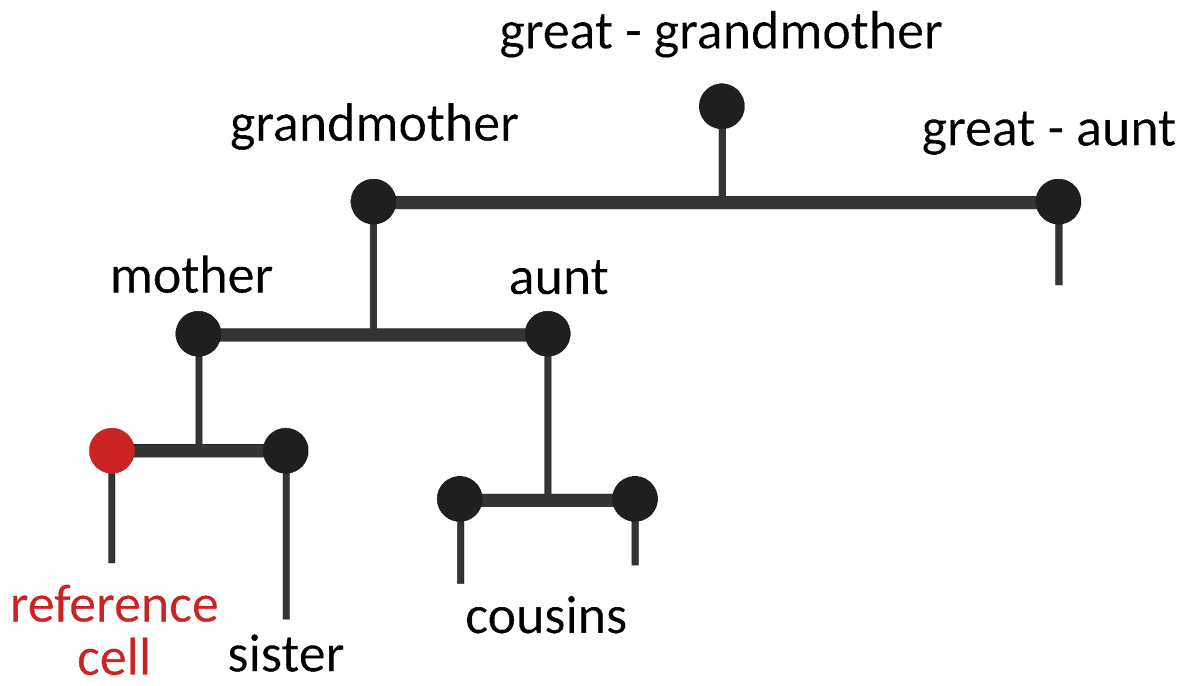
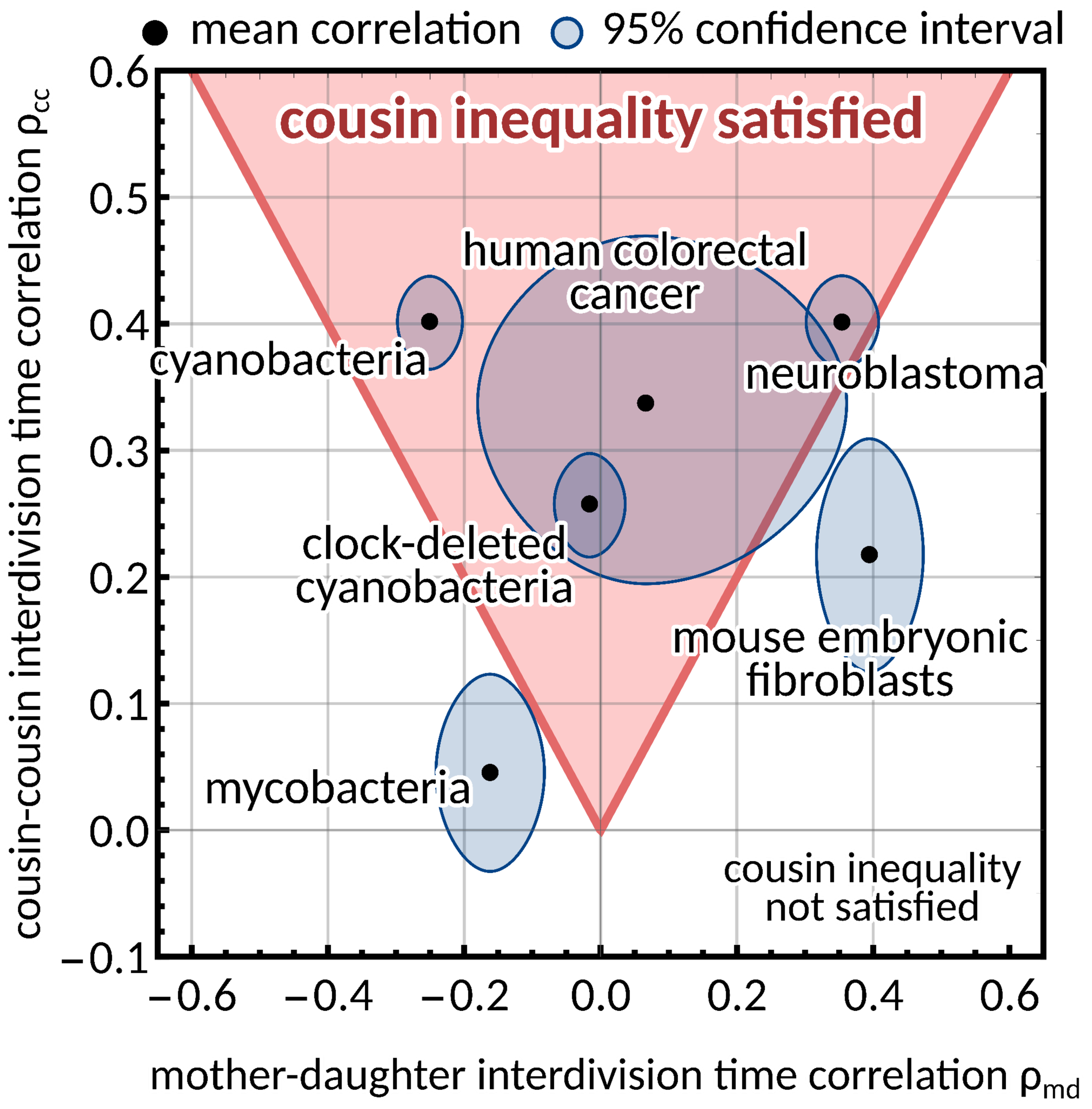
INTRODUCTION

How can different **interdivision time correlations** on **lineage trees** arise from **inheritance rules?**



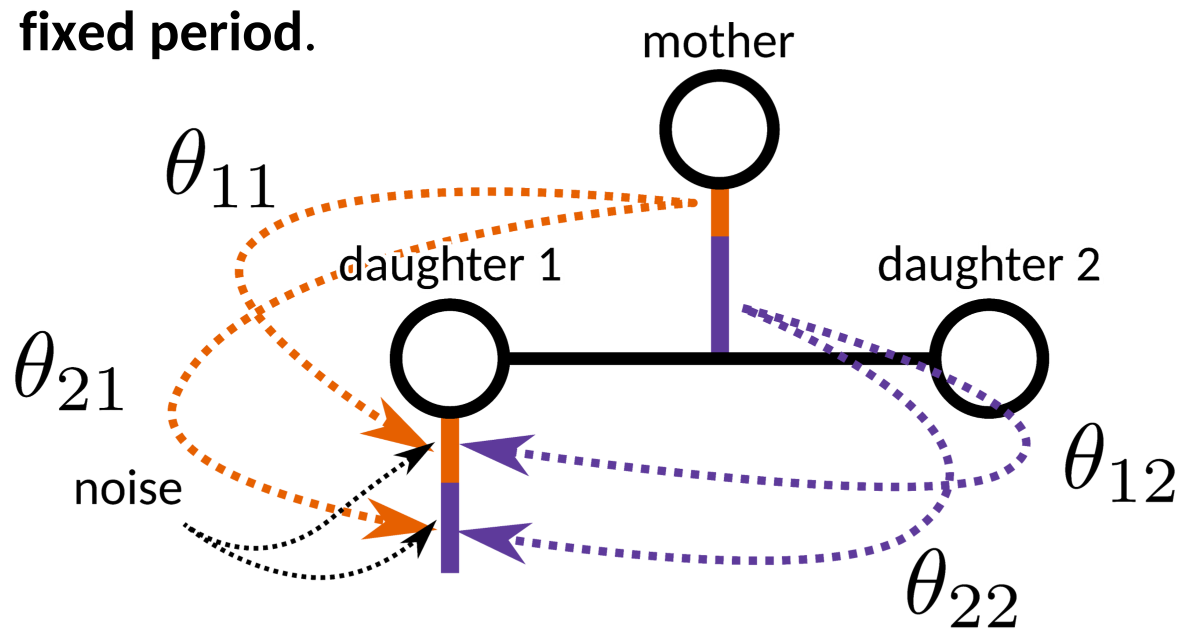
Using lineage tree data, we can compare cell information to other cells in the tree.

Cousin cells on a lineage tree can be **more correlated in interdivision time** than **mother-daughter pairs.** This cannot be explained by a simple model of interdivision time inheritance.



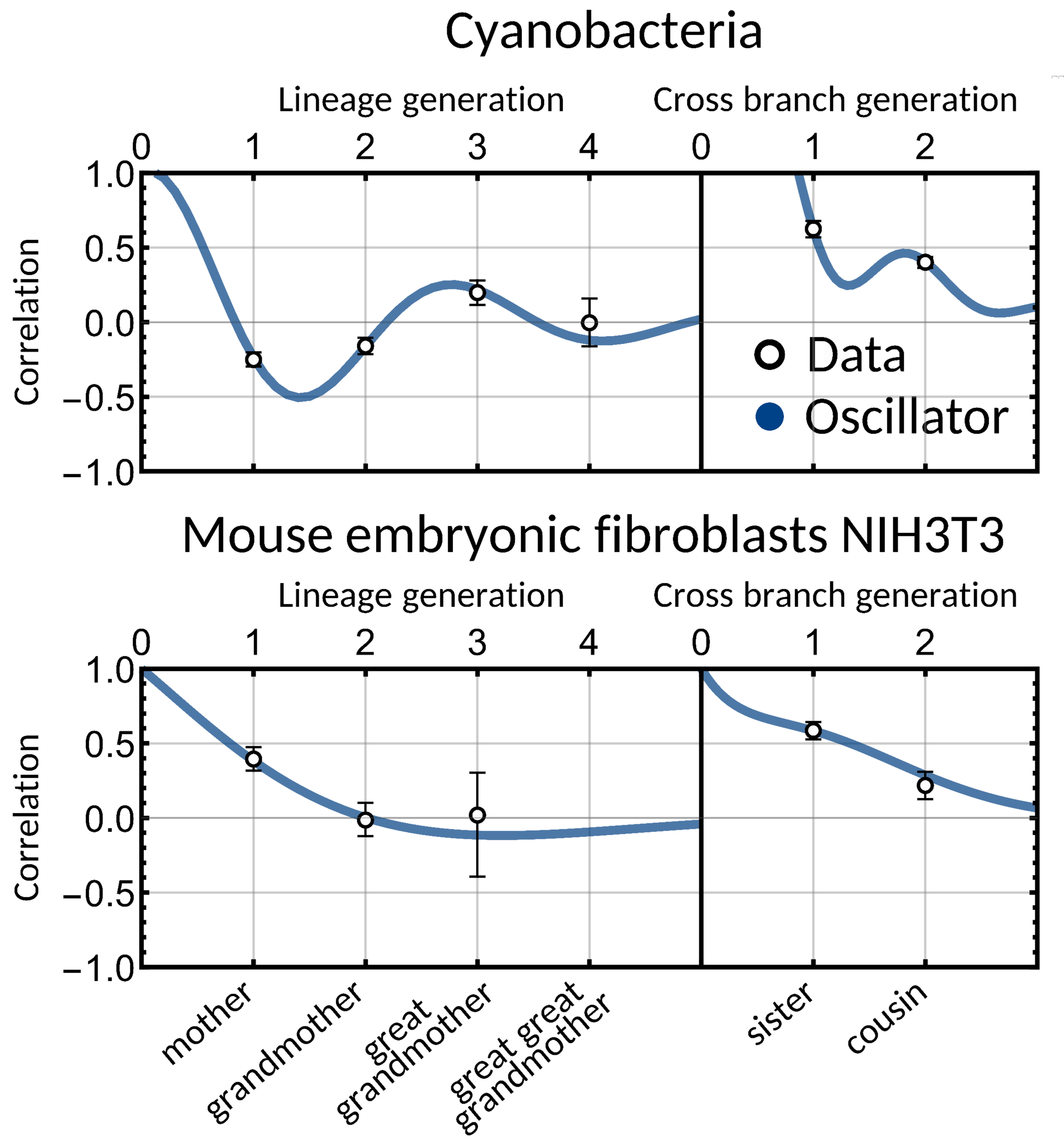
METHODS

Our **general stochastic matrix model** of abstract cell-cycle factor inheritance can satisfy the cousin inequality. We label one of the possible model behaviours **'oscillator' behaviour**, where the predicted correlations oscillate with some **fixed period**.



Model schematic (2D) showing how each factor in the mother cell influences the factors in the daughter cell.

Bayesian inference reveals that many different inheritance models produce the same correlation pattern seen in the data.

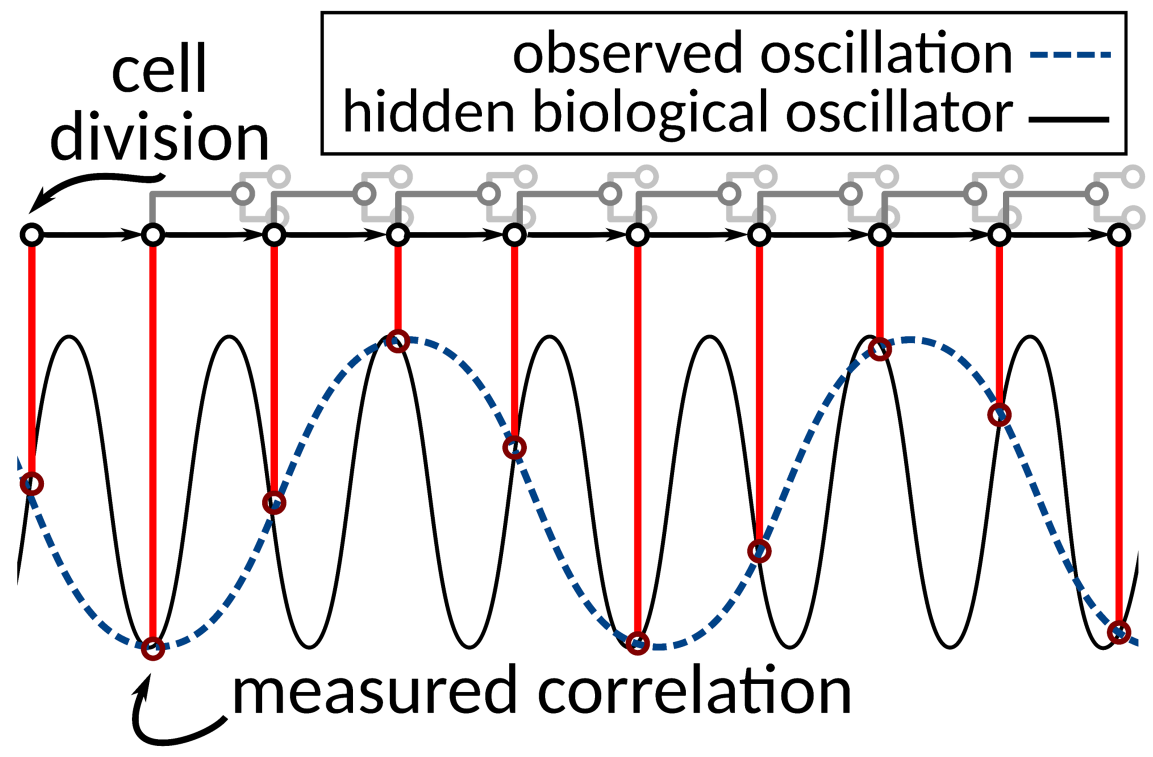


Model fit for cyanobacteria and mouse embryonic fibroblasts, exhibiting oscillatory behaviour. The oscillatory period is different for the two datasets.

We find that **oscillator behaviour gives a better fit** than the simple model for mouse embryonic fibroblasts, despite the **cousin inequality not being satisfied**.

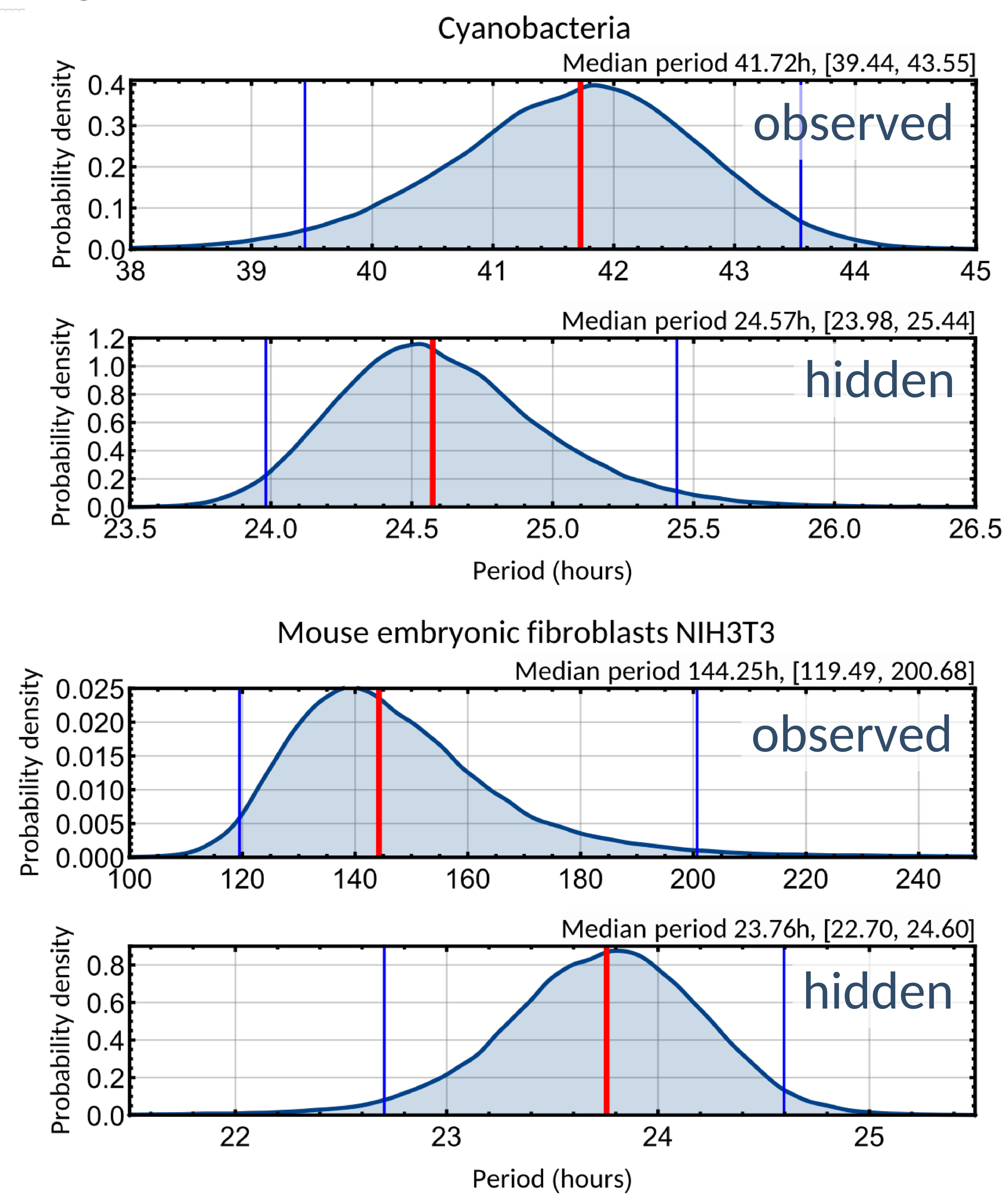
RESULTS

Could the observed oscillations have **biological interpretation?**



Sketch showing how a higher frequency oscillator can produce a lower frequency signal when sampled too infrequently.

For cyanobacteria and mouse embryonic fibroblasts, we reveal an approximately **24h period underlying oscillator**. This could be linked to **circadian rhythm**, which is known to regulate cell cycle in these cell types.



DATASETS:
Cyanobacteria and clock-deleted cyanobacteria – Martins et al. 2018 - *10.1073/pnas.1811309115*
Mycobacteria – Priestman et al. 2017 - *10.3389/fcell.2017.00064*
Human colorectal cancer HCT116 – Chakrabarti et al. 2018 - *10.1038/s41467-018-07788-5*
Neuroblastoma TET21N – Kuchen et al. 2020 - *10.7554/eLife.51002*
Mouse embryonic fibroblasts NIH3T3 – Mura et al. 2019 - *10.1371/journal.pcbi.1007054*

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