Correlated cousin cells and their link to cancer treatment

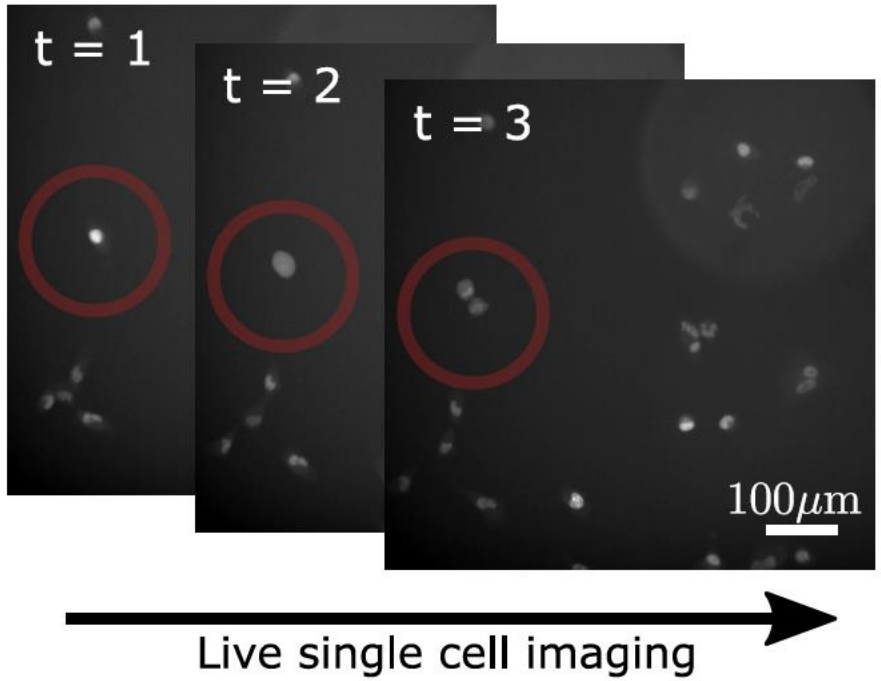
Fern Hughes

Supervisors: Dr Philipp Thomas & Dr Alexis Barr

Imperial College London

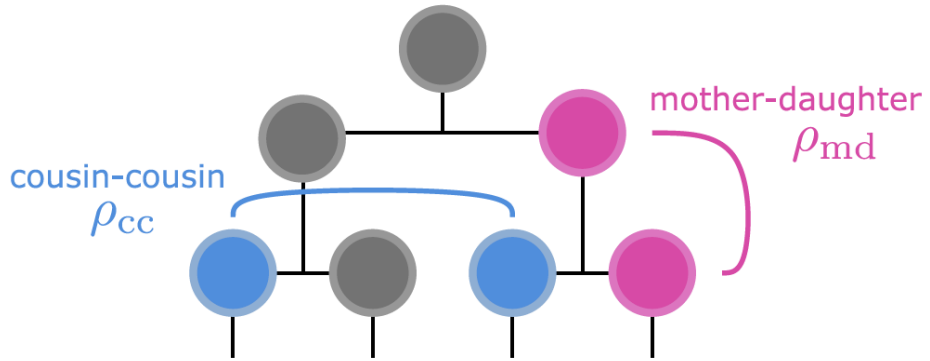
MRC London Institute of Medical Sciences

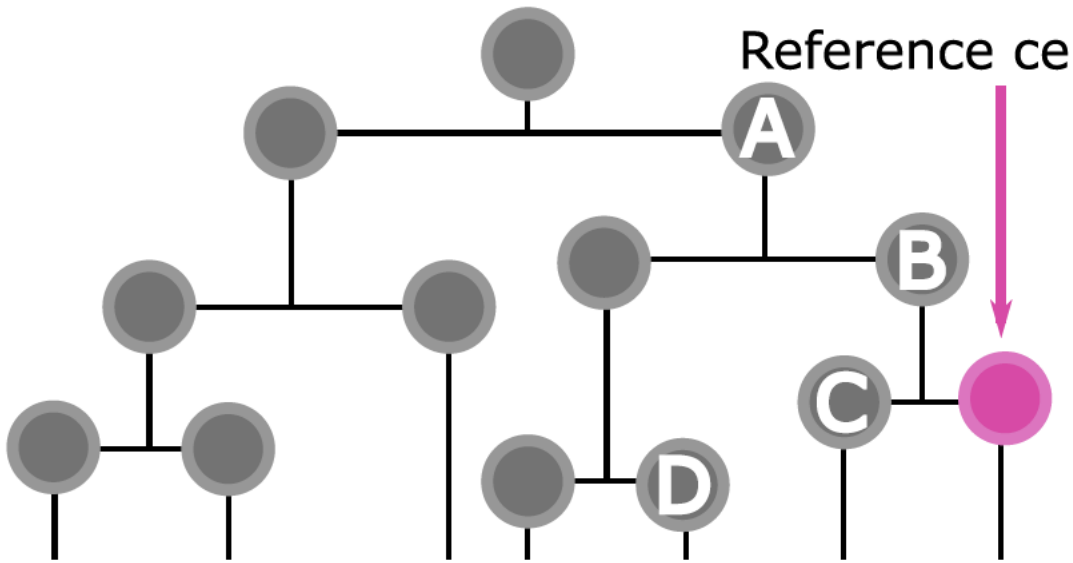
CMPH Centre for Mathematics of Precision Healthcare



Cousin inequality

$$\rho_{\mathrm{cc}} > |\rho_{\mathrm{md}}|$$



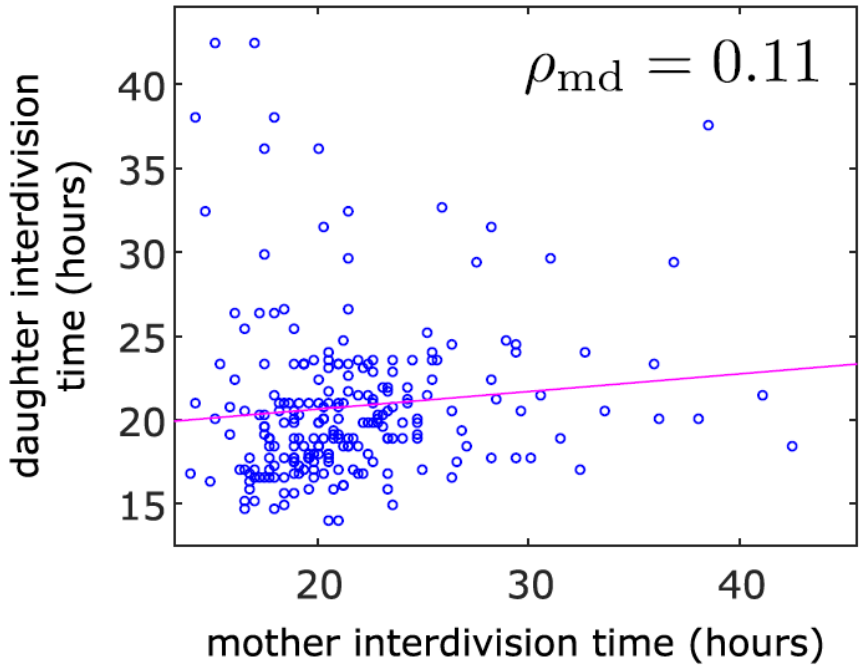


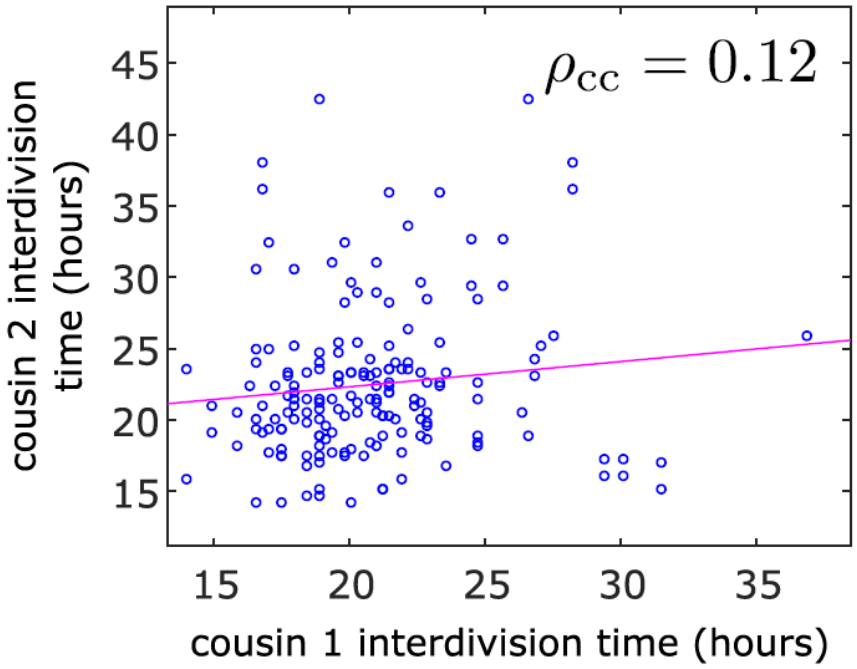
Lineage tree data

Relation to reference cell

A - grandmother
B - mother
C - sister
D - cousin

Non-small cell lung cancer A549





Human colon cancer HCT116
– Chakarbarti 2018

$\rho_{md} = 0.07 \quad \rho_{cc} = 0.35$

Neuroblastoma TET21N
– Kuchen 2020

$\rho_{md} = 0.35 \quad \rho_{cc} = 0.40$

$$\mathrm{d}_1 = \theta \cdot \mathrm{m} + z_{\mathrm{d}_1},$$
$$\mathrm{d}_2 = \theta \cdot \mathrm{m} + z_{\mathrm{d}_2}.$$

Cousin inequality

$$\rho_{\mathrm{cc}} > |\rho_{\mathrm{md}}|$$

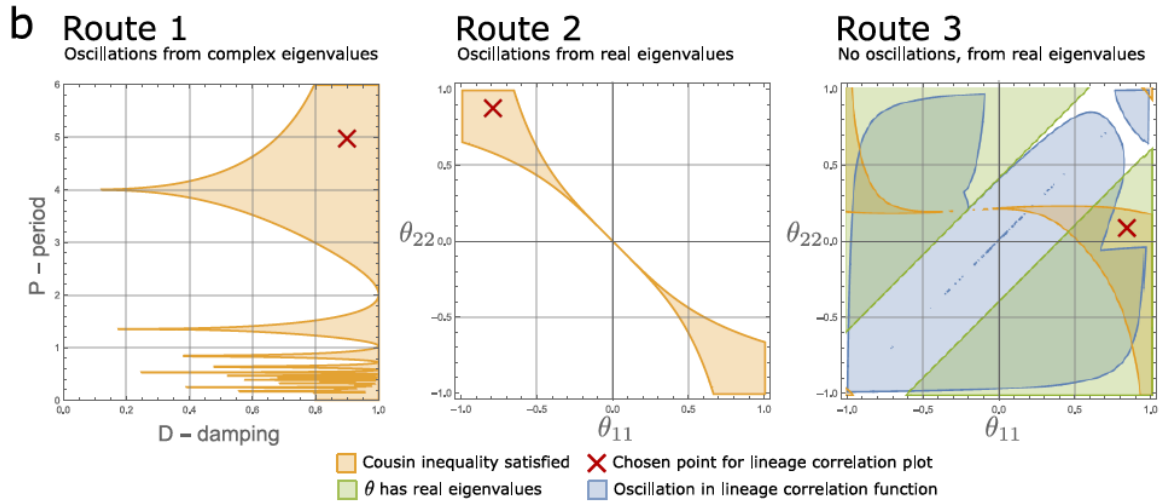
Cannot be satisfied

Cannot explain cell behaviour using simple inheritance rules.

Cell Systems
Article

Cell-Cycle Position of Single MYC-Driven Cancer Cells Dictates Their Susceptibility to a Chemotherapeutic Drug

Tatsiana Ryl,[1,2,5] Erika E. Kuchen,[1,2,5] Emma Bell,[3,5] Chunxuan Shao,[1,2] Andrés F. Flórez,[1,2] Gregor Mönke,[1,2,4] Sina Gogolin,[3] Mona Friedrich,[3] Florian Lamprecht,[1,2] Frank Westermann,[3,*] and Thomas Höfer[1,2,6,*]
[1]Division of Theoretical Systems Biology, German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany
[2]Bioquant Center, University of Heidelberg, 69120 Heidelberg, Germany
[3]Neuroblastoma Genomics, German Cancer Research Center (DKFZ), 69120 Heidelberg, Germany
[4]Present address: Developmental Biology Unit, European Molecular Biology Laboratory (EMBL), 69117 Heidelberg, Germany
[5]These authors contributed equally
[6]Lead Contact
*Correspondence: f.westermann@dkfz.de (F.W.), t.hoefer@dkfz.de (T.H.)
http://dx.doi.org/10.1016/j.cels.2017.07.005



$$\boldsymbol{d}_1 = \boldsymbol{\theta m} + \boldsymbol{z}_{d_1}$$
$$\boldsymbol{d}_2 = \boldsymbol{\theta m} + \boldsymbol{z}_{d_2}$$

$$\boldsymbol{d}_1 = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \qquad \boldsymbol{\theta} = \begin{pmatrix} \theta_{11} & \theta_{12} \\ \theta_{21} & \theta_{22} \end{pmatrix}$$

Total cell cycle duration calculated by $\tau = \boldsymbol{\alpha}^{\mathsf{T}}\boldsymbol{x}$ or $\tau = \alpha_1 x_1 + \alpha_2 x_2$

Split model
$\alpha_1 = \alpha_2 = 1$

Correlations between phases of the cell cycle

Which works the best?

Hidden model
$\alpha_1 = 1$ and $\alpha_2 = 0$

Correlations between cell cycle duration and a hidden factor