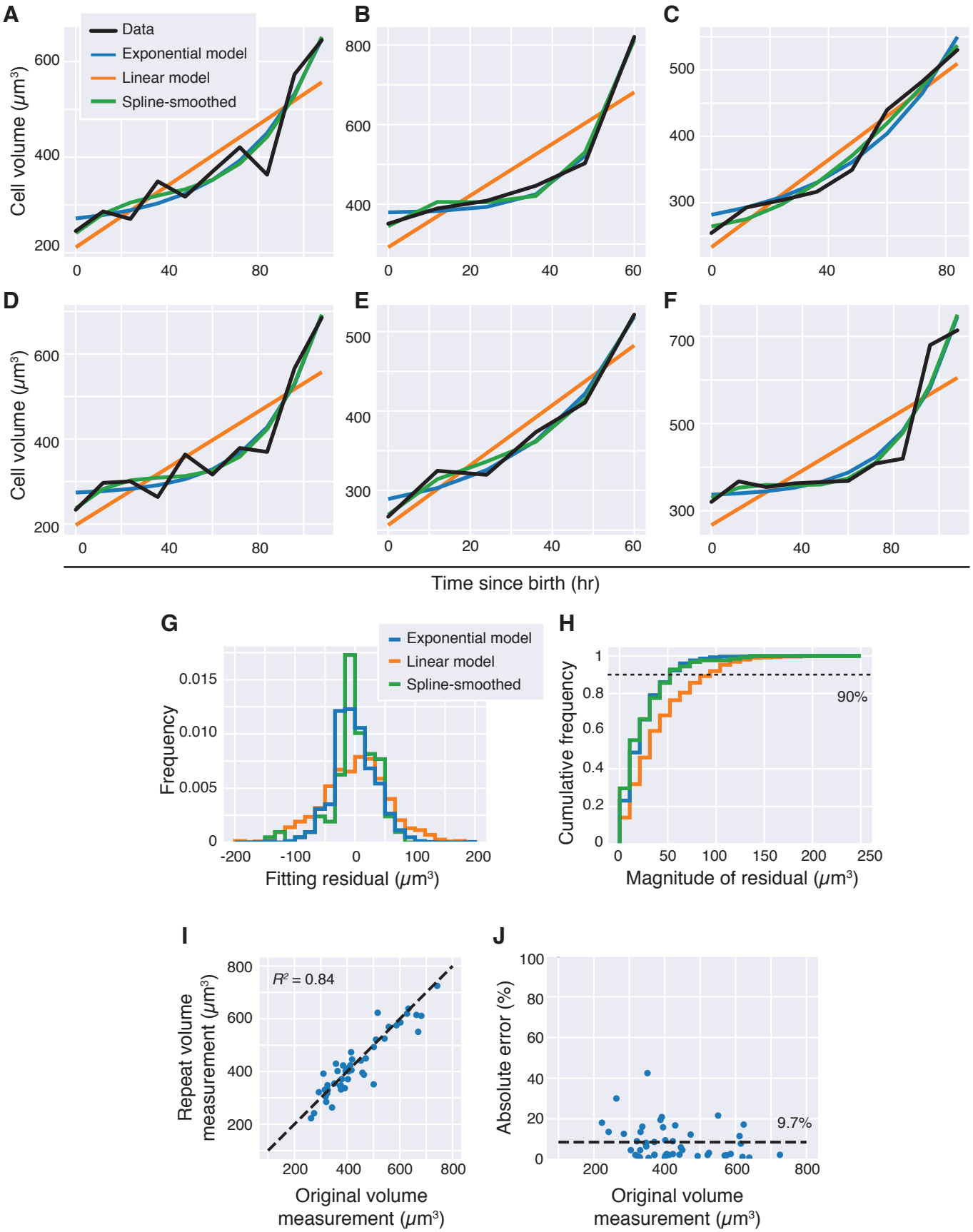

A
B
C
D
E
F
Data
Exponential model
Linear model
Spline-smoothed
Cell volume (μm³)
Time since birth (hr)
G
Frequency
Fitting residual (μm³)
H
Cumulative frequency
90%
Magnitude of residual (μm³)
I
R² = 0.84
Repeat volume measurement (μm³)
Original volume measurement (μm³)
J
Absolute error (%)
9.7%
Original volume measurement (μm³)

Methods S1, Figure i. Cell growth curves and segmentation noise.

A-F. Examples of individual volume growth curves. The fits to linear (orange), exponential (blue), and cubic smoothing spline (green) models are shown. The empirical data is shown in black.

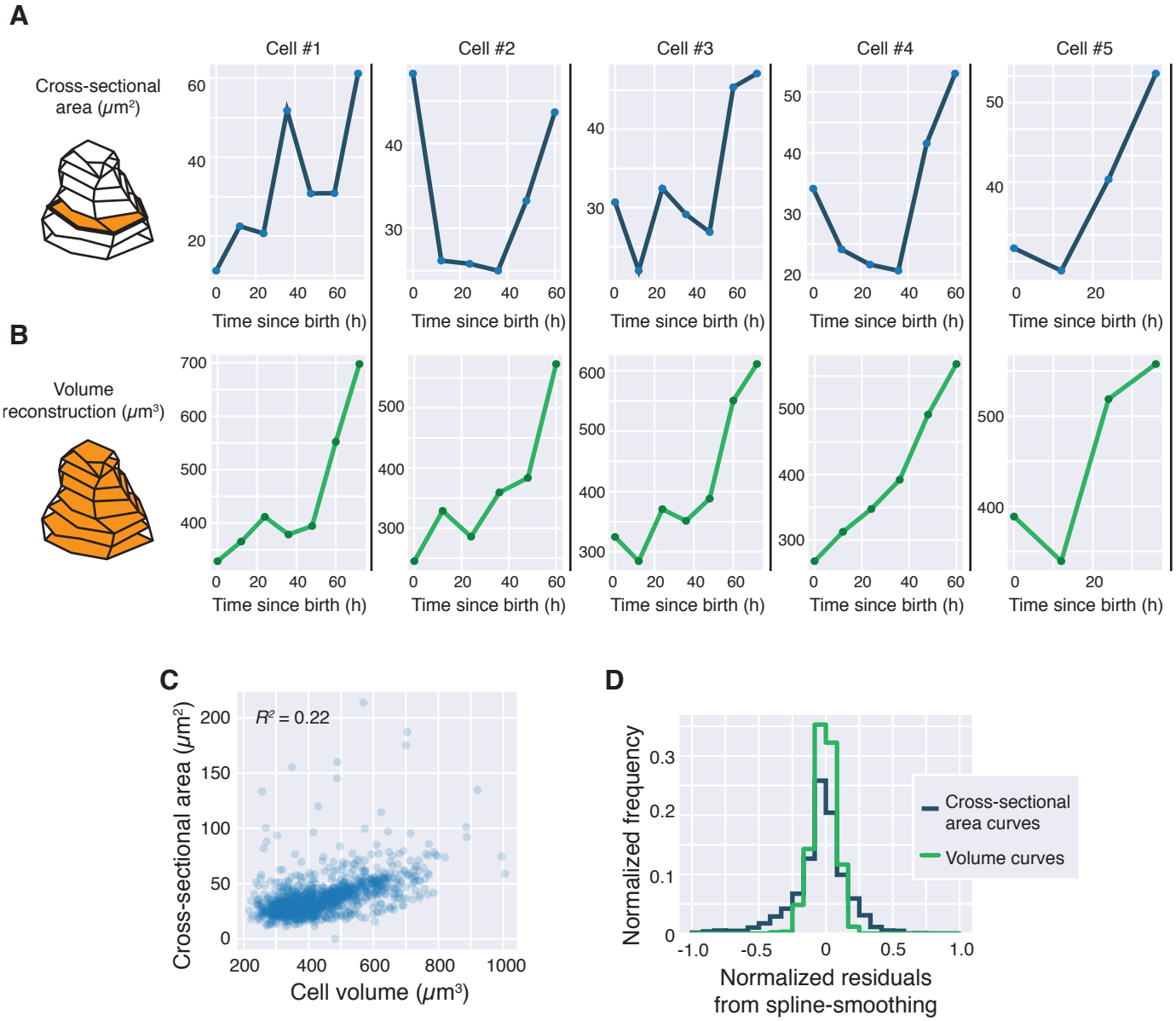
G. The distribution of fitting residuals from linear, exponential, and smoothing spline fits (N = 1,159).

H. The cumulative distribution of the magnitude of residuals. The dotted line denotes the 90% cumulative probability.

I. The difference in Bayes information criterion (BIC) score for exponential and linear models for each cell. Lower BIC score indicates a better model.

J. Intra-user variation in cell volume reconstruction for 48 independent time-points. The dotted line is the identity.

K. The intra-user absolute error rate, defined as the absolute difference between repeat and original measurements normalized by the original volume measurement. The average error of 9.7% is shown as a dotted line.


A
Cell #1
Cell #2
Cell #3
Cell #4
Cell #5
Cross-sectional area (μm²)
Time since birth (h)
B
Volume reconstruction (μm³)
Time since birth (h)
C
R² = 0.22
Cross-sectional area (μm²)
Cell volume (μm³)
D
Normalized frequency
Cross-sectional area curves
Volume curves
Normalized residuals from spline-smoothing

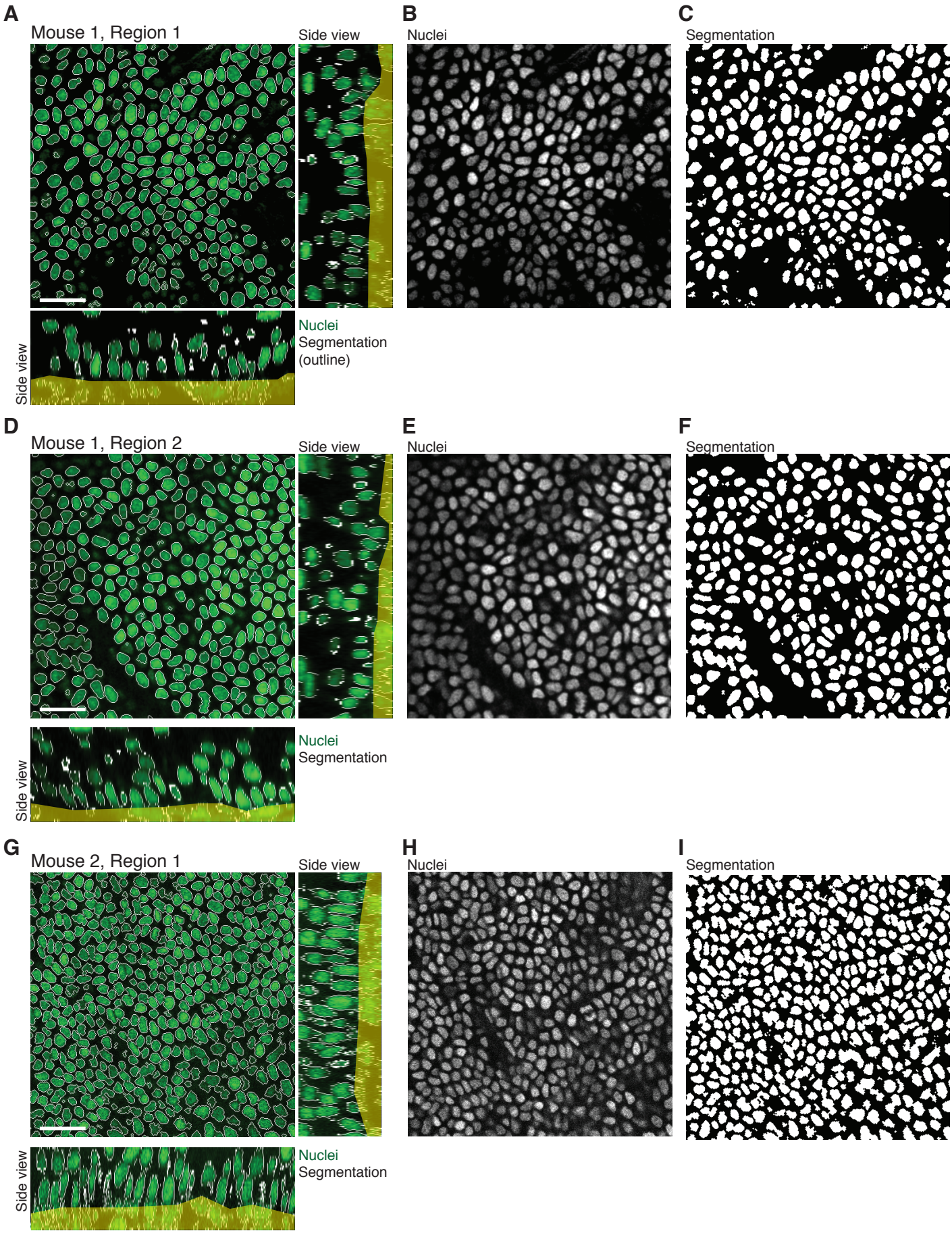
Methods S1, Figure ii. Comparison of cross-sectional area and cell volume as estimates for cell size.

A. Five representative growth curves of the cross-sectional cell area through an entire cell cycle.

B. The cell volume growth curves for the same five cells shown in (A).

C. The correlation between cross-sectional area and cell volume ($N = 827$).

D. The magnitudes of the normalized residuals (residuals normalized by the empirical data) from fitting area growth curves (blue) or volume growth curves (green) to smoothing splines. The magnitudes of normalized residuals are larger for cross-sectional area measurements than for volume measurements ($P < 10^{-15}$, one-tailed two-sample KS-test).

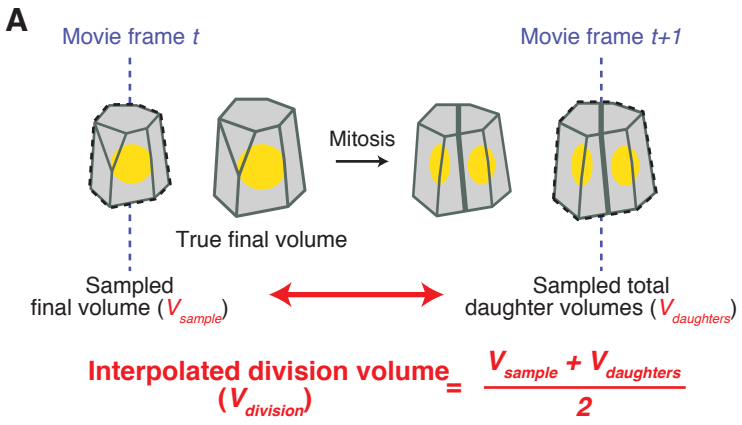

A
Mouse 1, Region 1
Side view
Nuclei
Segmentation
(outline)
Side view
B
Nuclei
C
Segmentation
D
Mouse 1, Region 2
Side view
Nuclei
Segmentation
Side view
E
Nuclei
F
Segmentation
G
Mouse 2, Region 1
Side view
Nuclei
Segmentation
Side view
H
Nuclei
I
Segmentation

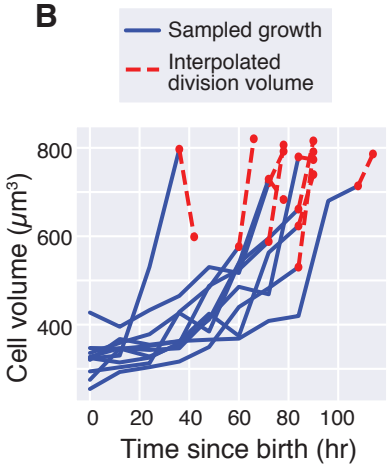
Methods S1, Figure iii. Nuclear segmentation for nuclear volume reconstruction.

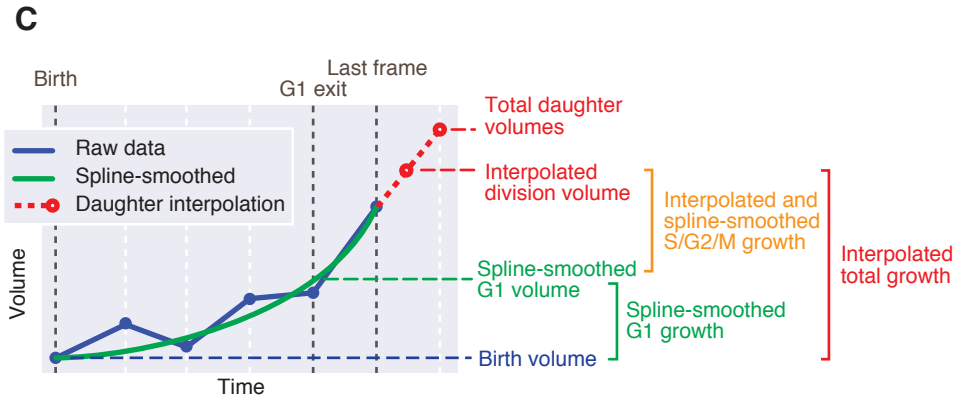
A, D, G. The results of automatic nuclear segmentation for the three independent regions. The H2B-Cerulean nuclear reporter is shown in green. The thresholded outlines are shown in white. *En face* views and side views are shown. The dermis underneath the basal layer (non-epidermal tissue) is masked out in yellow.

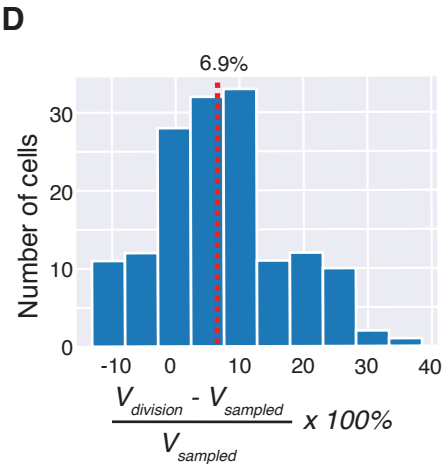
B, E, H. The H2B-Cerulean nuclear reporter images.

C, F, I. The nuclear masks generated by automatic thresholding of the H2B-Cerulean signal.


A
Movie frame t
Movie frame t+1
Mitosis
True final volume
Sampled final volume (V sample)
Sampled total daughter volumes (V daughters)
Interpolated division volume (V division) = V sample + V daughters / 2


B
Sampled growth
Interpolated division volume
Cell volume (μm³)
800
600
400
0
20
40
60
80
100
Time since birth (hr)


C
Birth
Last frame
G1 exit
Raw data
Spline-smoothed
Daughter interpolation
Volume
Time
Total daughter volumes
Interpolated division volume
Spline-smoothed G1 volume
Birth volume
Interpolated and spline-smoothed S/G2/M growth
Spline-smoothed G1 growth
Interpolated total growth


D
6.9%
Number of cells
30
20
10
0
-10
0
10
20
30
40
V division - V sampled / V sampled x 100%

Methods S1, Figure iv. Estimating final cell division volume.

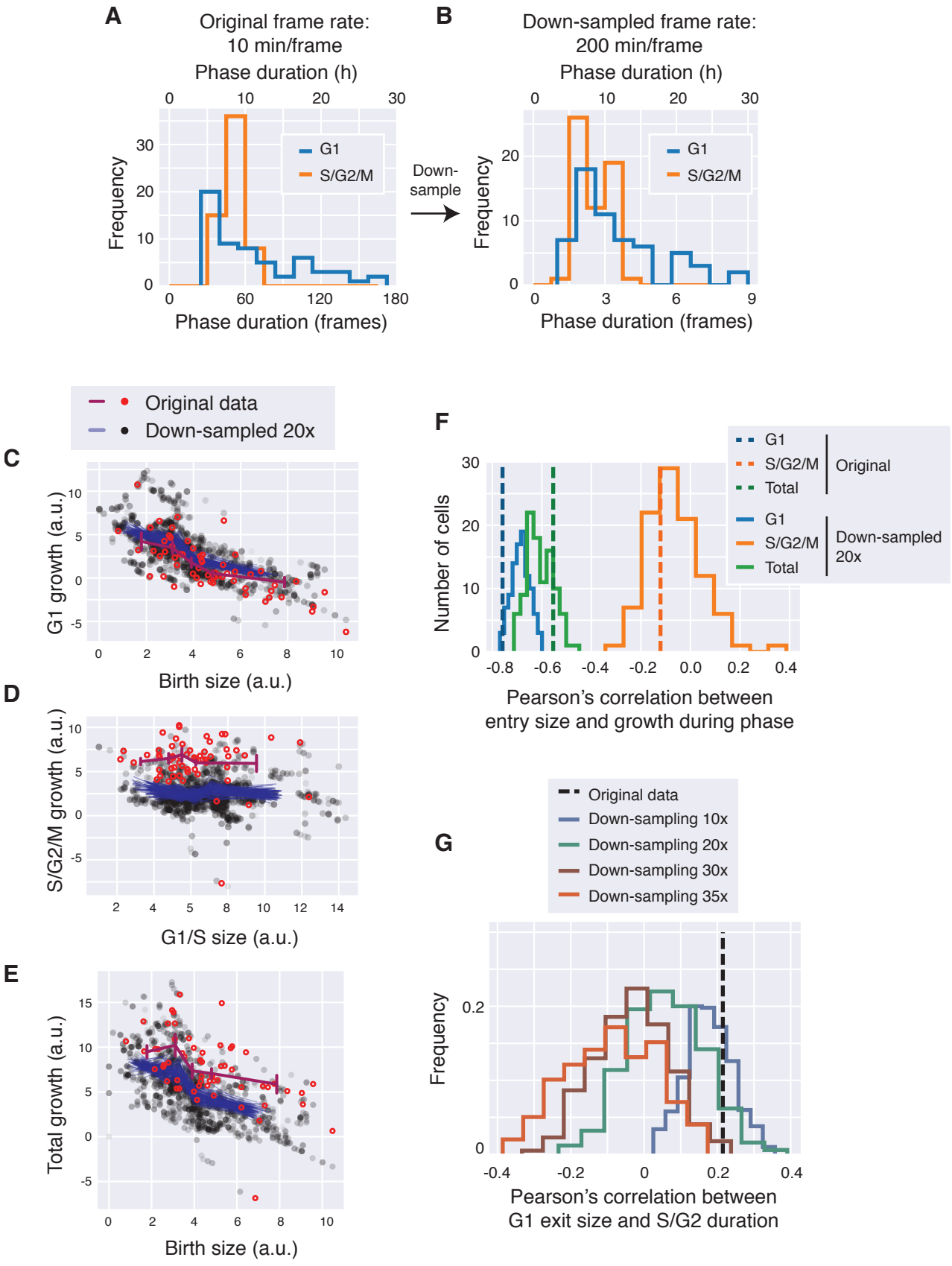
A. Schematic of interpolated division volume estimation. We took the average between the sampled final volume and the sum of the volume of the two daughter cells.

B. The cell volume growth curves are shown for ten representative cells, where the interpolated division volume is shown in red.

C. Schematic of cell volume estimations used in **Figure 3**. We fit the data to a smoothing spline to estimate G1 exit volume. We use the interpolated division volume as defined in (A).

D. The distribution of the difference between sampled and interpolated division volumes, normalized by the sampled volume. Dotted line denotes the mean.

Related to **Figure 2, 3**.


A
Original frame rate:
10 min/frame
Phase duration (h)
Frequency
Phase duration (frames)
G1
S/G2/M
B
Down-sampled frame rate:
200 min/frame
Phase duration (h)
Down-sample
Frequency
Phase duration (frames)
G1
S/G2/M
C
Original data
Down-sampled 20x
G1 growth (a.u.)
Birth size (a.u.)
D
S/G2/M growth (a.u.)
G1/S size (a.u.)
E
Total growth (a.u.)
Birth size (a.u.)
F
Number of cells
Pearson's correlation between
entry size and growth during phase
G1
S/G2/M
Total
Original
Down-sampled
20x
G
Original data
Down-sampling 10x
Down-sampling 20x
Down-sampling 30x
Down-sampling 35x
Frequency
Pearson's correlation between
G1 exit size and S/G2 duration

Methods S1, Figure v. Estimating the effect of low temporal resolution on size control correlations.

A. The distribution of cell cycle phase durations of HMECs growing *in vitro* from {Berenson:2019ff}. The corresponding number of frames is shown.

B. The data in (A) were down-sampled 20-fold so that we had the same number of time points as the *in vivo* data. Compare with **Figure 2C**.

C-E. Cell size control correlations are shown for HMECs comparing original and down-sampled data. Original data are shown in red, while the ensemble of 500 randomly down-sampled data are shown in black. The solid lines denote binned mean data for original (red) or down-sampled (blue) data. Cell size is measured from the cell size reporter generated by {Berenson:2019ff}. Birth size is plotted against G1 growth in (C). Cell size at G1/S is plotted against S/G2 growth in (D). Birth size is plotted against total growth in (E).

F. The Pearson's correlation (R) between the cell size at the indicated phase-entry and growth during the indicated phase are shown for G1 (blue), S/G2 (orange), and the total cell cycle (green). The distribution of R from randomly down-sampled data are shown in solid lines. Dotted lines denote the value of R in the original data for their corresponding colors. R for S/G2 phase in particular shows a broader distribution in the down-sampled data.

G. The Pearson's correlation (R) between G1 exit size and S/G2 duration for increasing down-sampling factors. Dotted line indicates the R in the original data. As the temporal sampling becomes poorer, the distribution of R shifts left, indicating a spurious negative correlation may be introduced by poor temporal sampling.