Boundary driven growth

Simulated tumor

a

Position in the tumor center results in slow cell growth rate

1

Mean birth rate

1.0

0.5

Y

X

2

Position on the tumor periphery permits cell to grow fast

Tumor time tree

b

Center-trapped lineage has no recent sampled divisions, leading to long terminal branch

1

Peripheral lineage with fast growth rate has recent common ancestor with sister lineage

2

Time to target tumor size

Tumor genetic tree

c

Few divisions in center-bound lineage leads to low mutation accumulation

1

Many divisions in peripheral lineage leads to high mutation accumulation

2

Genetic distance

Unrestricted growth

d

Tumor position uncorrelated with growth rate

3

Mean birth rate

1.0

0.5

Y

X

e

3

More uniform growth rate leads to less variable terminal branch lengths

Time to target tumor size

f

3

More uniform growth rate leads to less variable mutational accumulation

Genetic distance

g

Faster growth rate

Fast branching tree structure

More mutation accumulation

Slower growth rate

Slow branching tree structure

Less mutation accumulation

h

Var(TBL) Fig. 1B = 0.027

Var(TBL) Fig. 1E = 0.004

Terminal branch length (TBL)

Variance(Terminal branch length)

0.03

0.02

0.01

Boundary Driven   Unrestricted

i

Var(CR) Fig. 1C = 0.070

Var(CR) Fig. 1F = 0.034

Clock rate (CR)

Variance(Lineage clock rate)

0.075

0.050

0.025

Boundary Driven   Unrestricted