No Vein No Gain: Modeling Angiogenesis

Group 13
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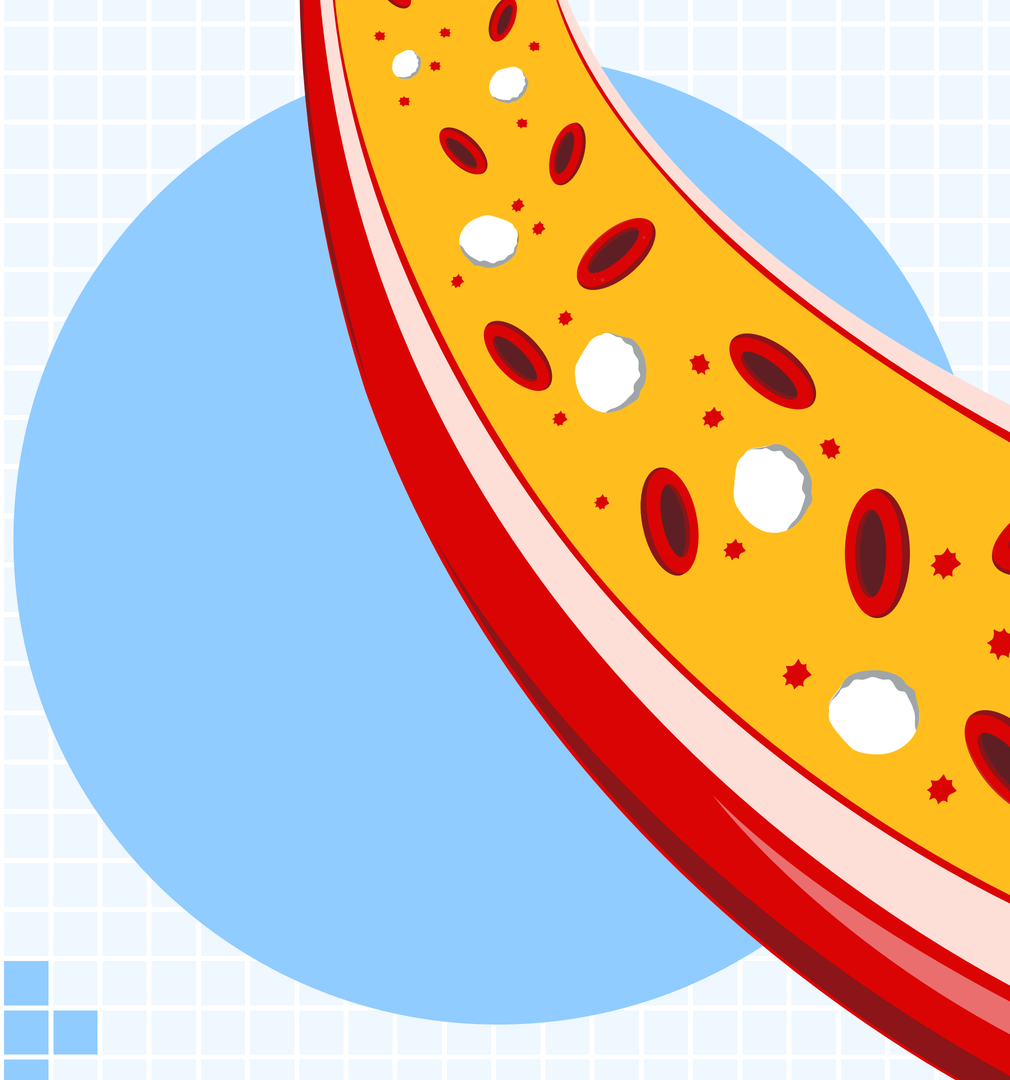
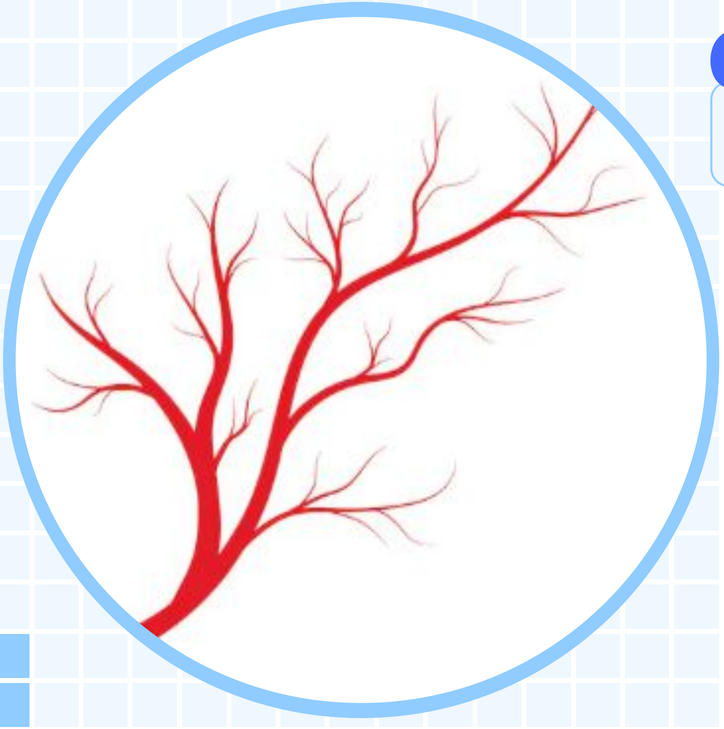


01

Background

Modeling Angiogenesis:
Understanding Tumor Growth through VEGF Dynamics

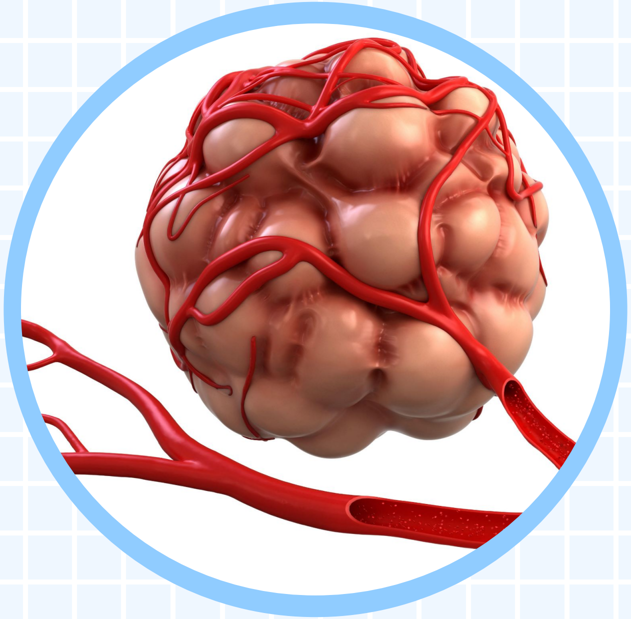
What to examine?



Angiogenesis: the growth of blood vessels.

- ➔ Scale-invariance
- ➔ Power law
- ➔ Various control parameters

VEGF and Tumor Growth



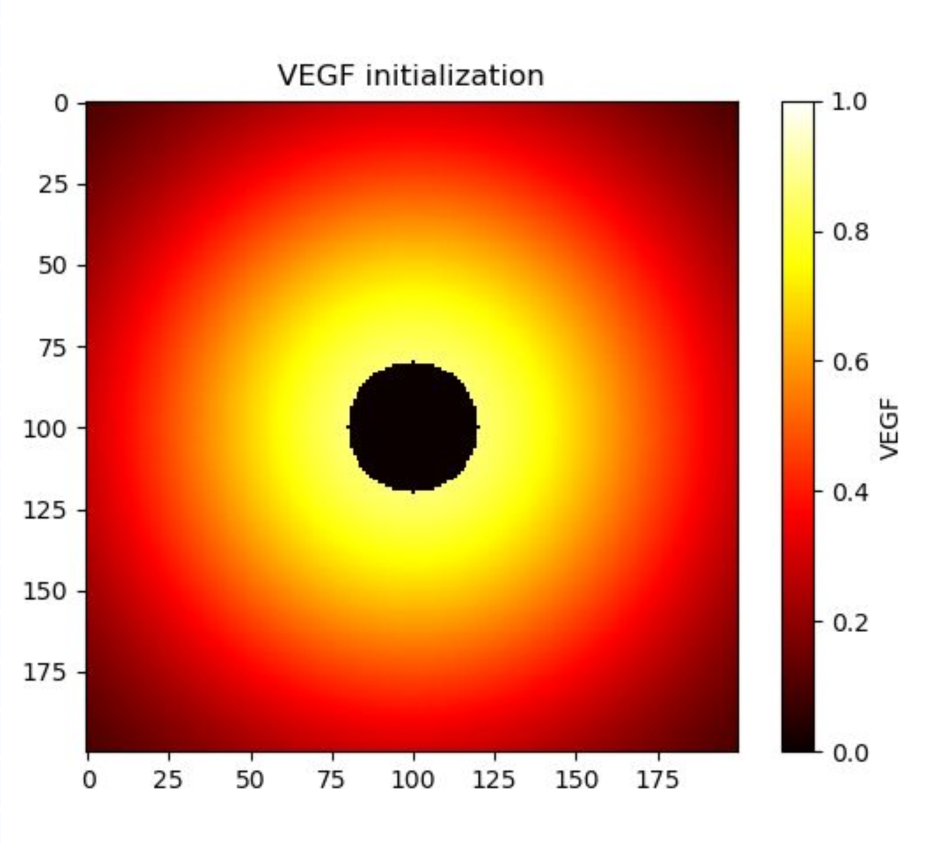
- ➔ Vascular endothelial growth factor (**VEGF**)
- ➔ Signaling molecule
- ➔ VEGF-based bias
- ➔ Eventually tumor growth

02

Model Design and Implementation

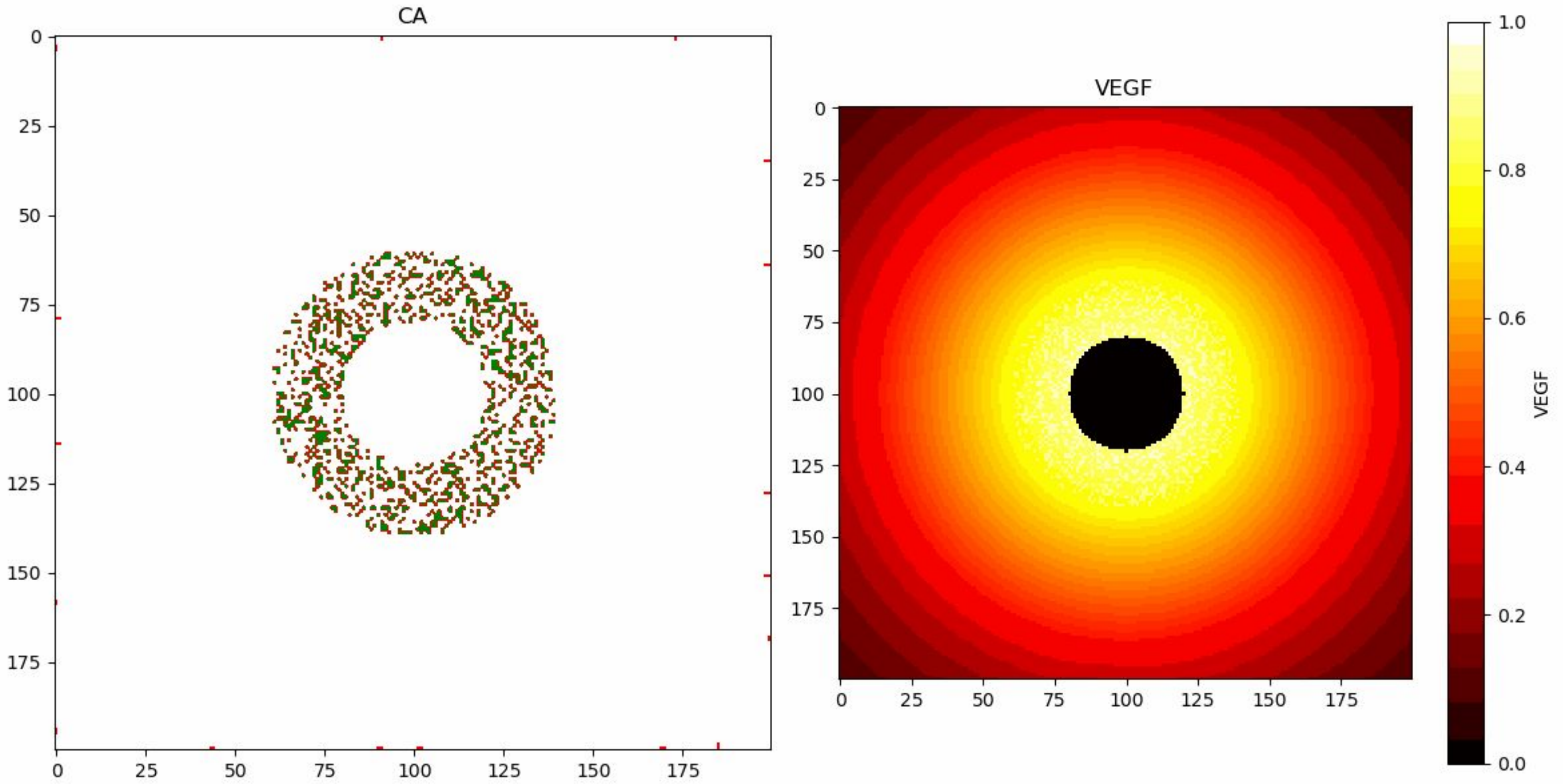
Modeling Angiogenesis:
Understanding Tumor Growth through VEGF Dynamics

Initialization



Initial VEGF values on background grid

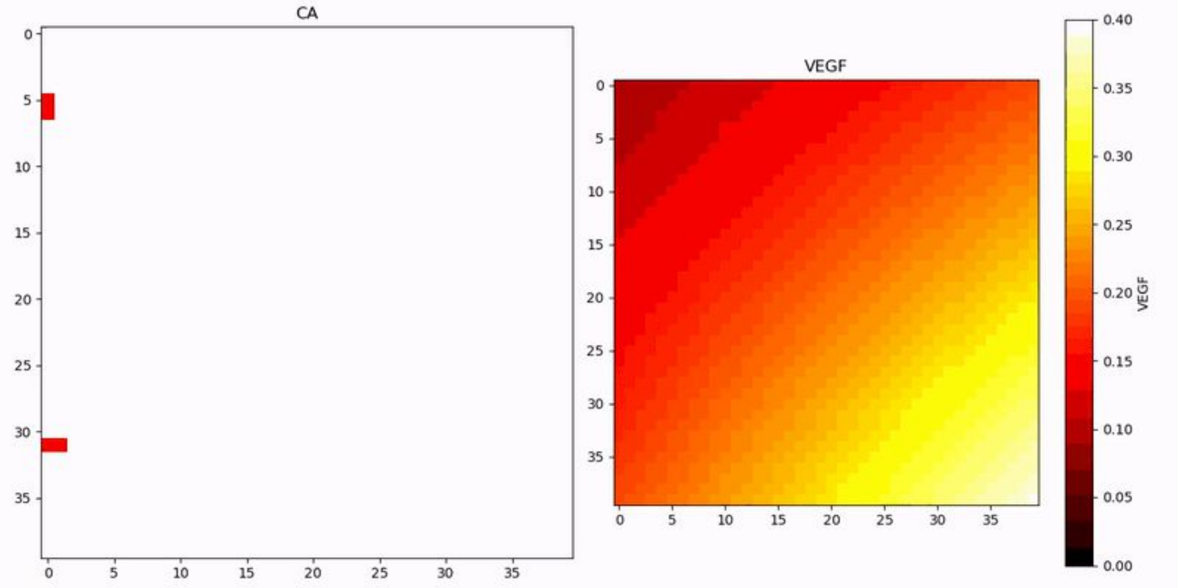
The Model

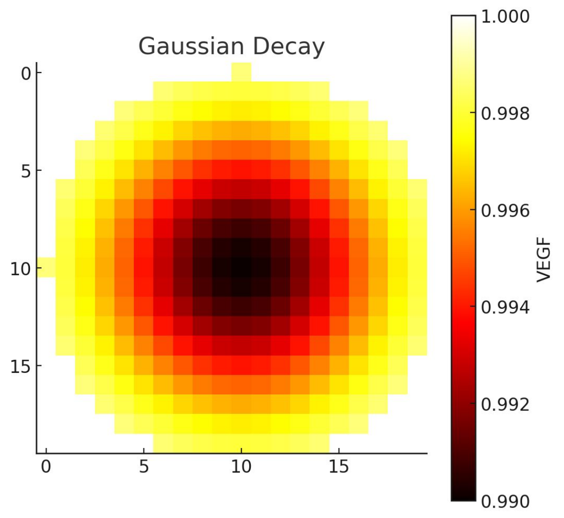

CA
0
25
50
75
100
125
150
175
0
25
50
75
100
125
150
175
VEGF
0
25
50
75
100
125
150
175
0
25
50
75
100
125
150
175
1.0
0.8
0.6
0.4
0.2
0.0
VEGF

Vessel Growth and Gaussian VEGF Decay

Probability of growing to neighbor cell x,y

*P(x,y) = U(0,1) * (1 - bias_factor) + VEGF(x,y) * bias_factor*





$$w(d) = e^{-\frac{d^2}{2\sigma^2}} \qquad \sigma = 10/2, \qquad d = 10$$

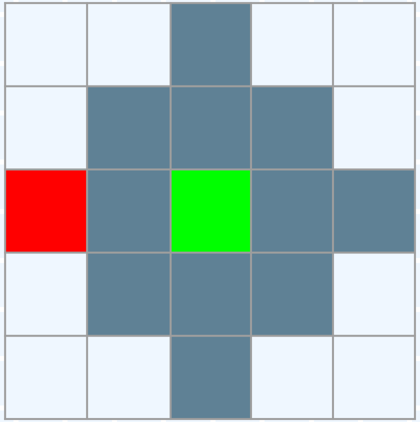
*VEGF(x,y) = max(0, VEGF(x,y) * (1 - w(d) * 0.01)*

Growth and Death of Proliferating Tumor Cells

$$P(static) = 1 - p$$
$$P(death) = p \times (1 - blood\_bias)$$
$$P(division) = p \times blood\_bias$$

$$blood\_bias(N) = \frac{1}{1 + e^{-(N - midpoint)}}$$

Von Neumann
Neighborhood
(r = 2)



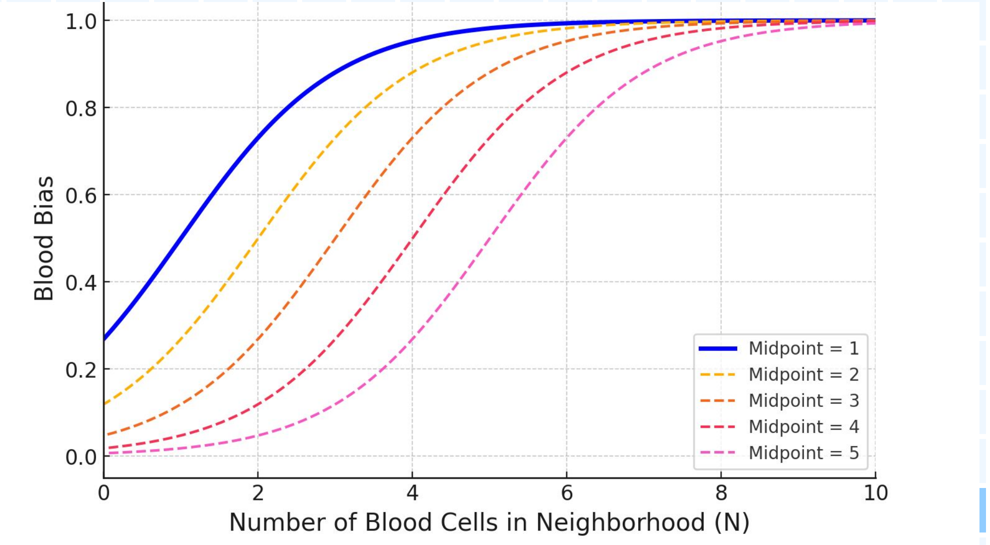
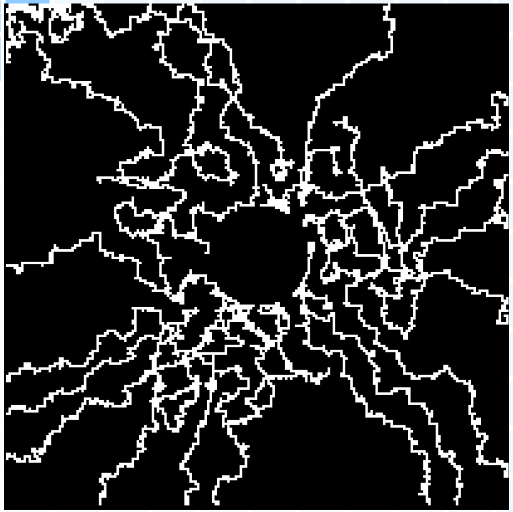
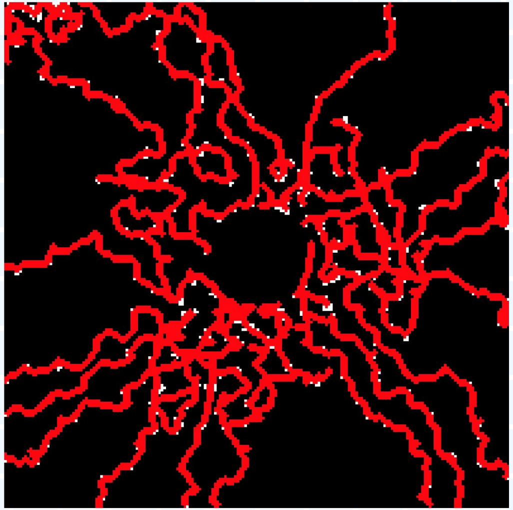


Image Processing and Vessel Network Creation

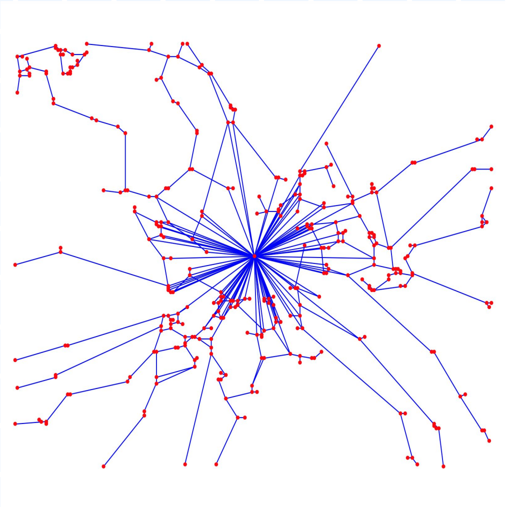
Binary Image



Skeletonized Image



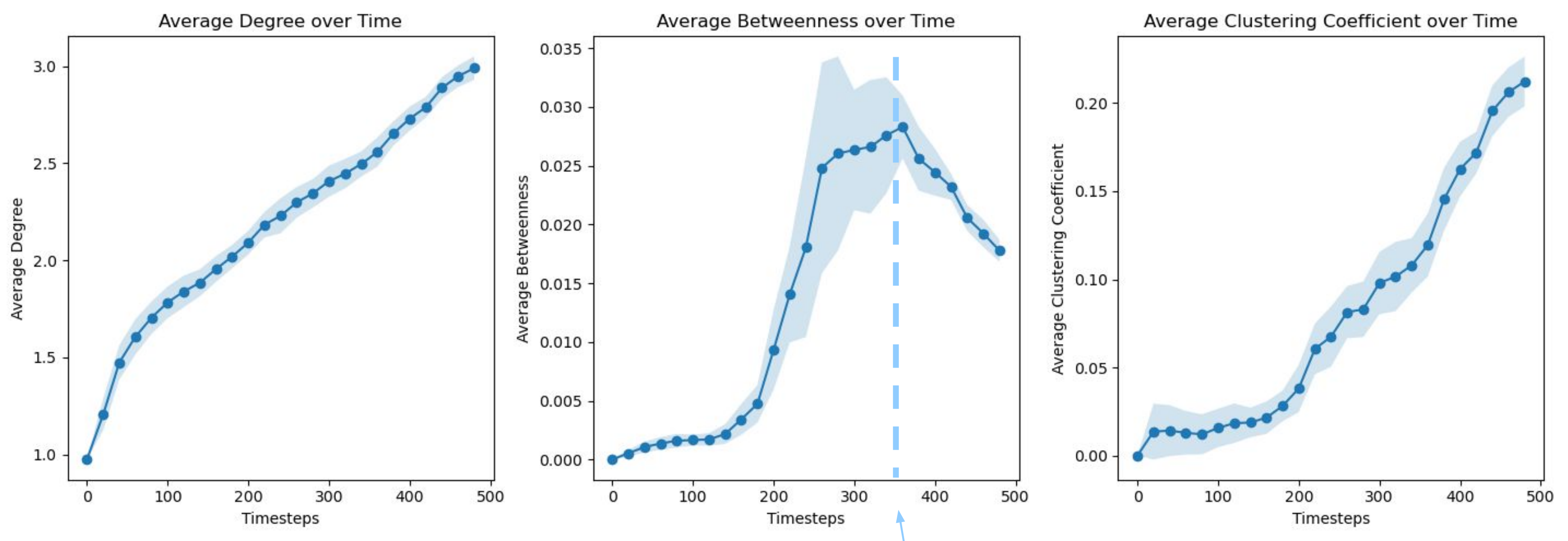
Estimated Network



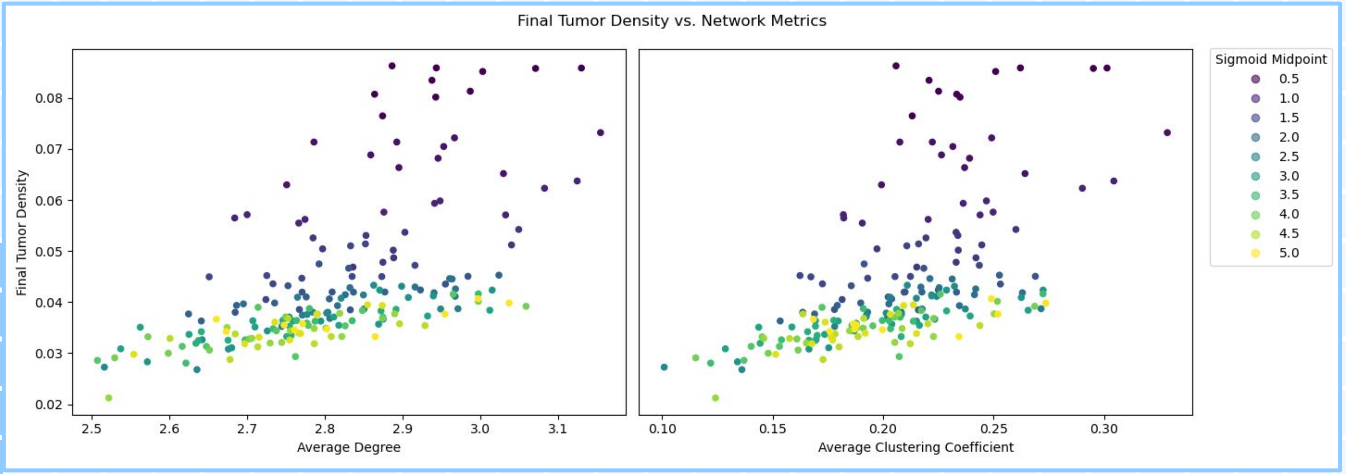
03

Results: Tumor and Vessel Growth Analysis

Network Measures over Time



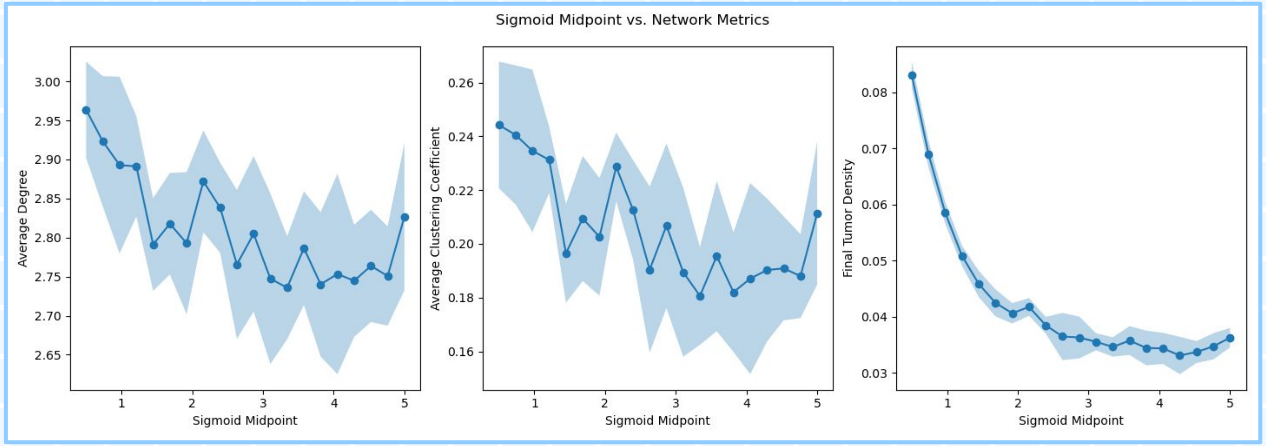
breakpoint



Tumor density VS Network Metrics

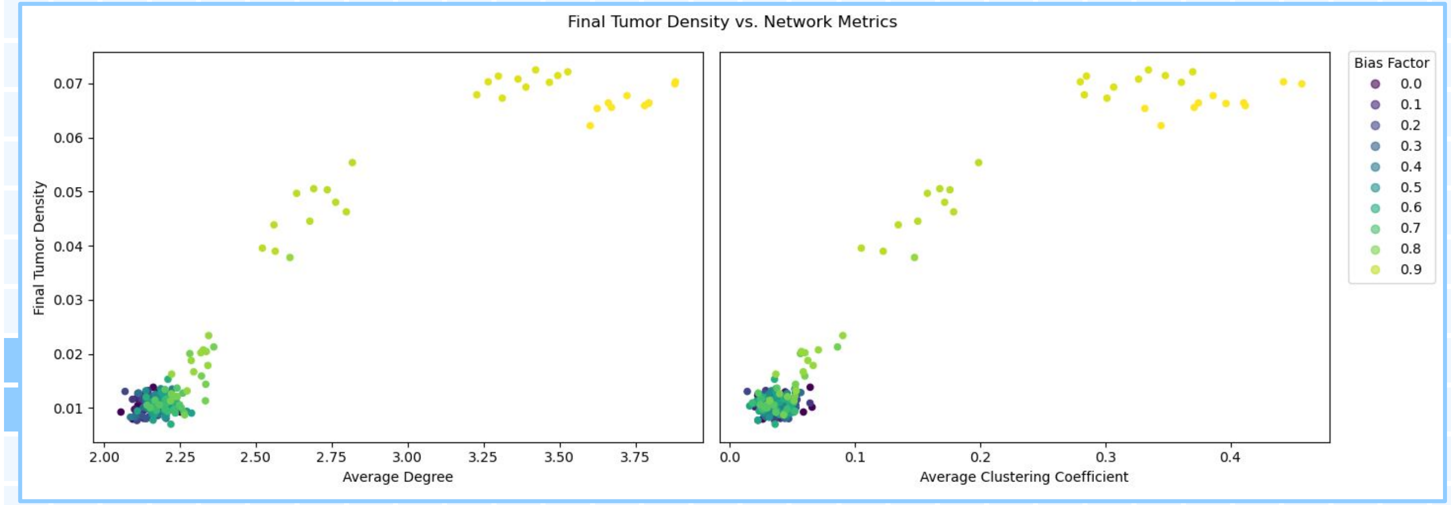
Varying Sigmoid Midpoint

Sigmoid Midpoint VS Network Metrics



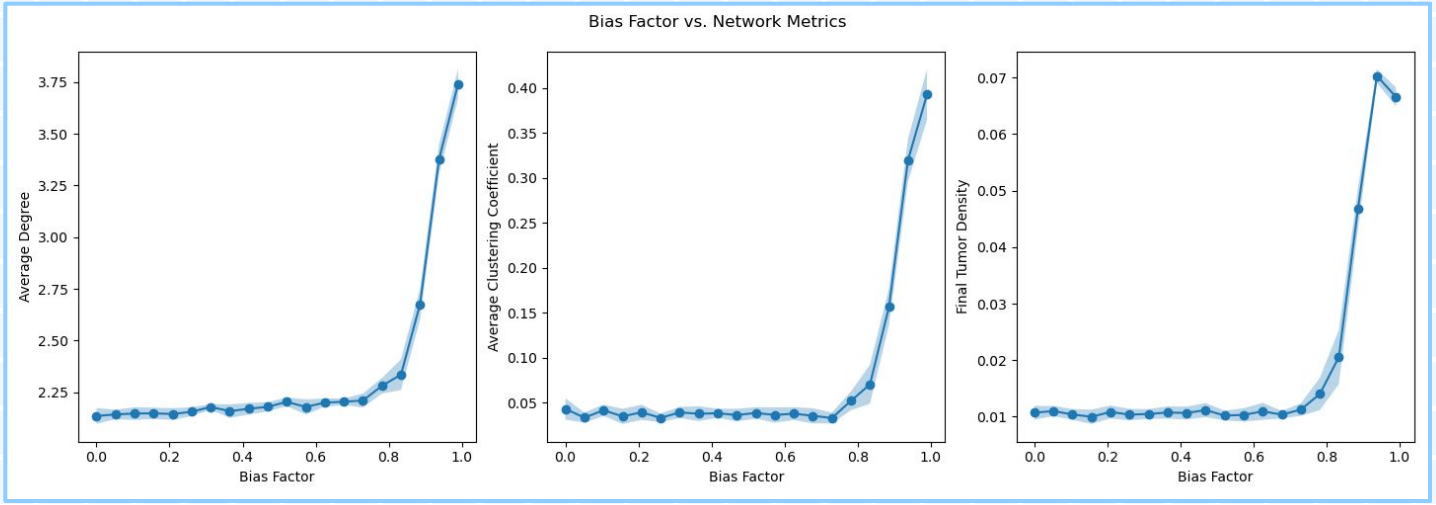
$$P(death) = p \times (1 - blood\_bias)$$

$$blood\_bias(N) = \frac{1}{1 + e^{-(N - \boxed{midpoint})}}$$



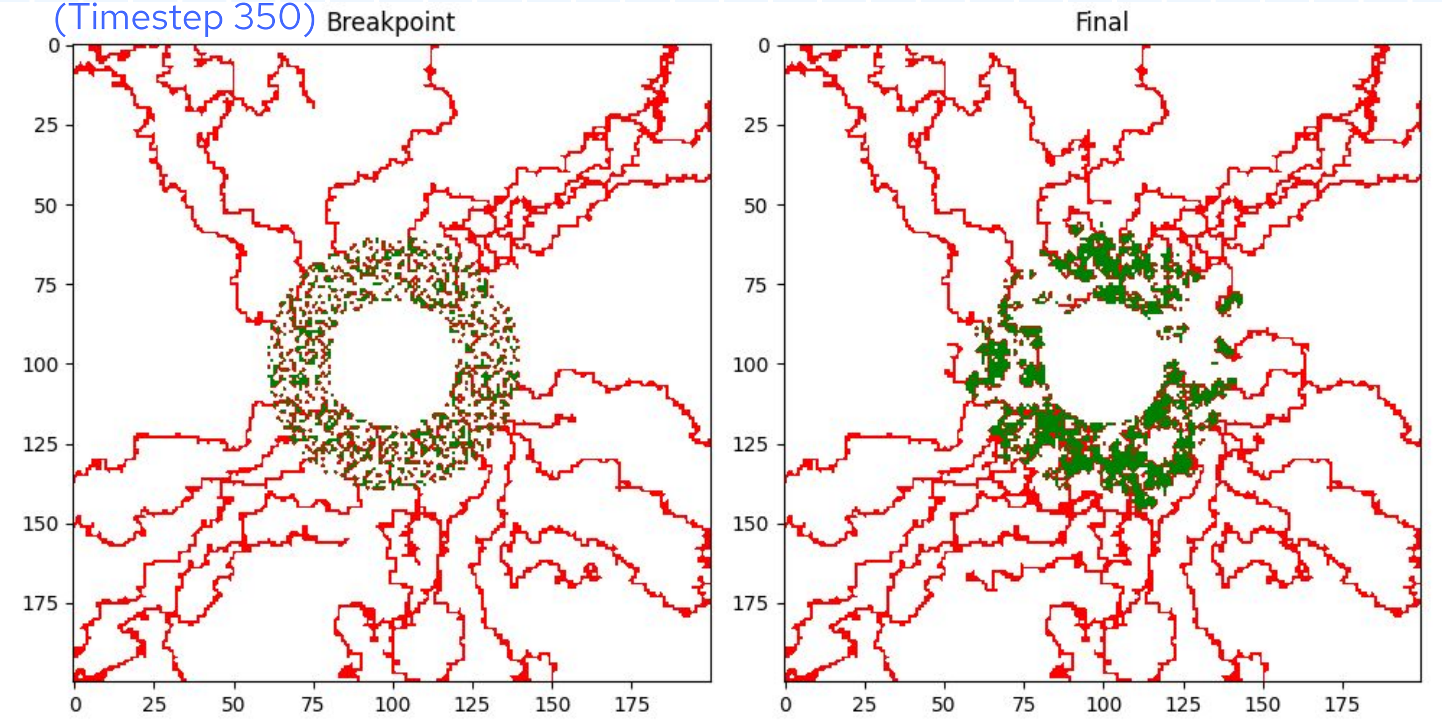
Tumor density VS Network metrics

Varying Bias Factor

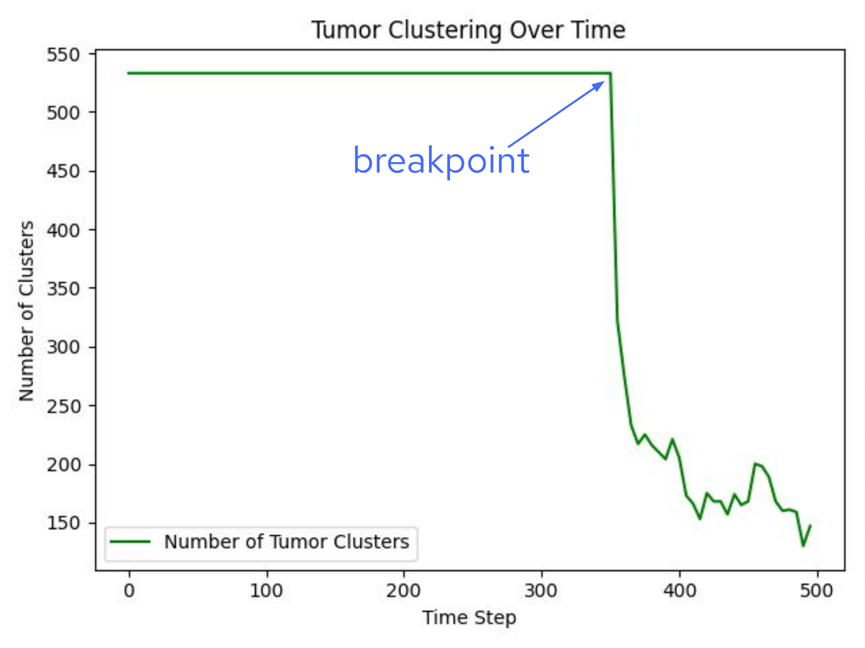


Bias factor VS Network Metrics

Tumor and Vessel Growth:
clustering behavior over time



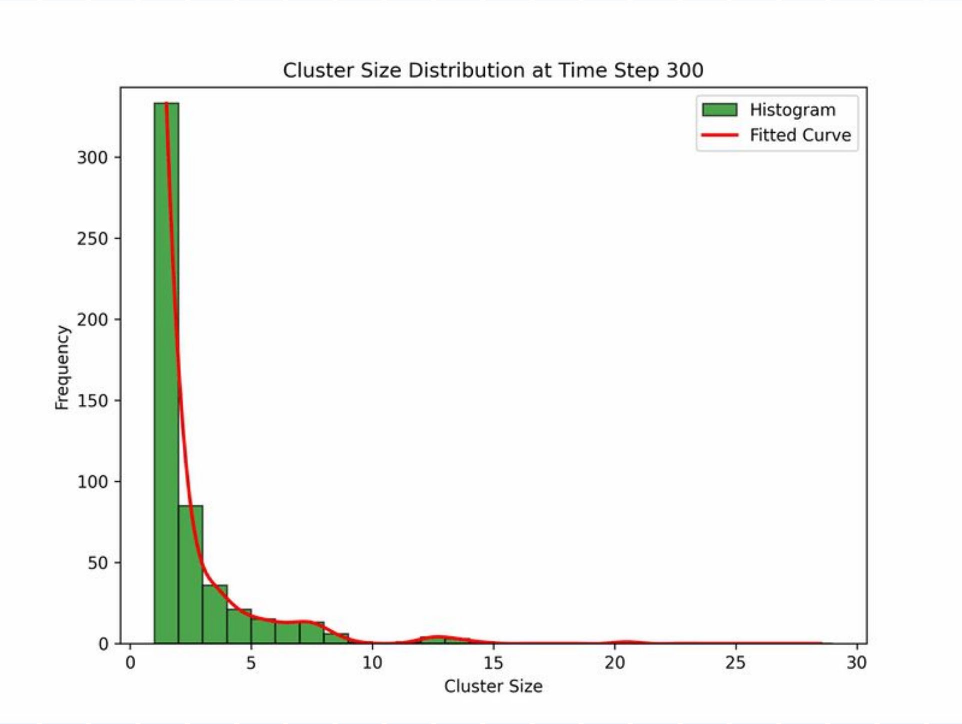
Tumor Growth:
clustering behavior over time



Minimum cluster size = 1

- ➔ Before the breakpoint, many small clusters exist.
- ➔ After the breakpoint, clusters start to merge.

Tumor Growth:
clustering behavior over time

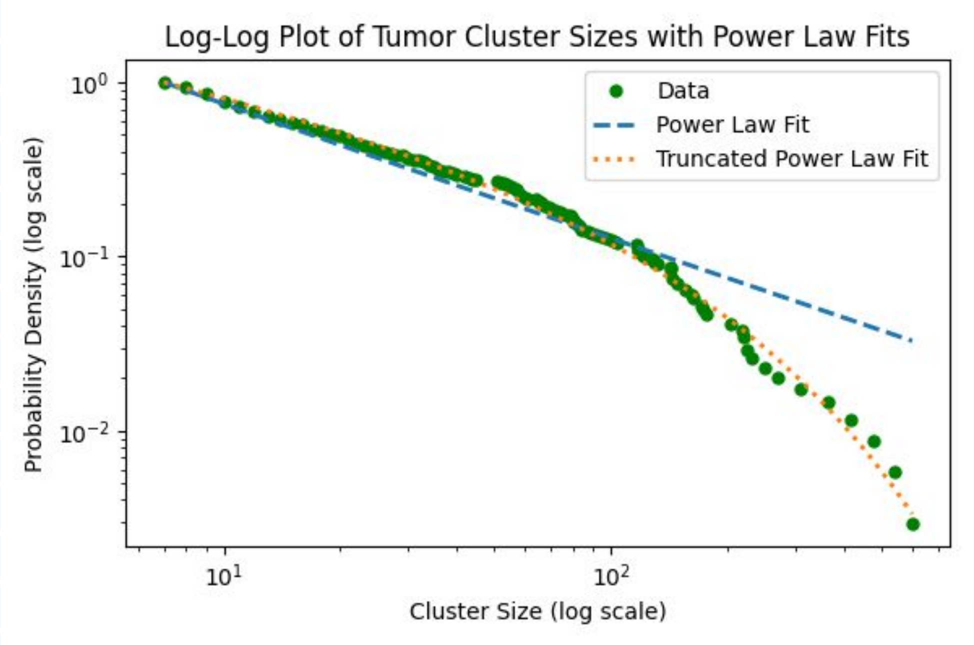


Power law?
Truncated power law?

- ➔ 100 simulations.
- ➔ 10 combined datasets per simulation.

```
Proportion of Power Law: 0.00%
Proportion of Truncated Power Law: 97.00%
```

Tumor Growth:
clustering behavior over time

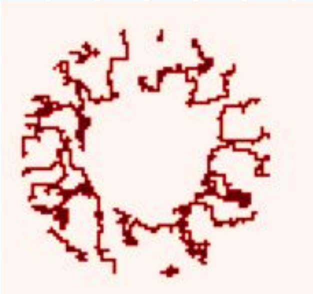


Tumor cells clusters follow a truncated power law distribution.

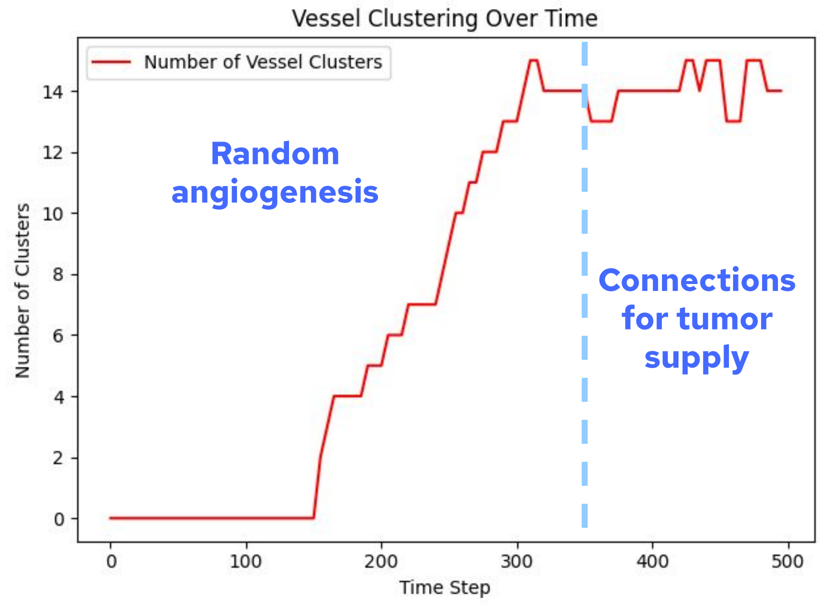
Truncated Power law VS	R	p-value
Exponential	5.56	<<0.05
Lognormal	3.30	<<0.05
Power law	3.99	<<0.05

Vessel Growth:
clustering behavior over time

- ➔ Study the cluster distribution of vessel cells.
- ➔ Restrict the view **only in the tumor area.**

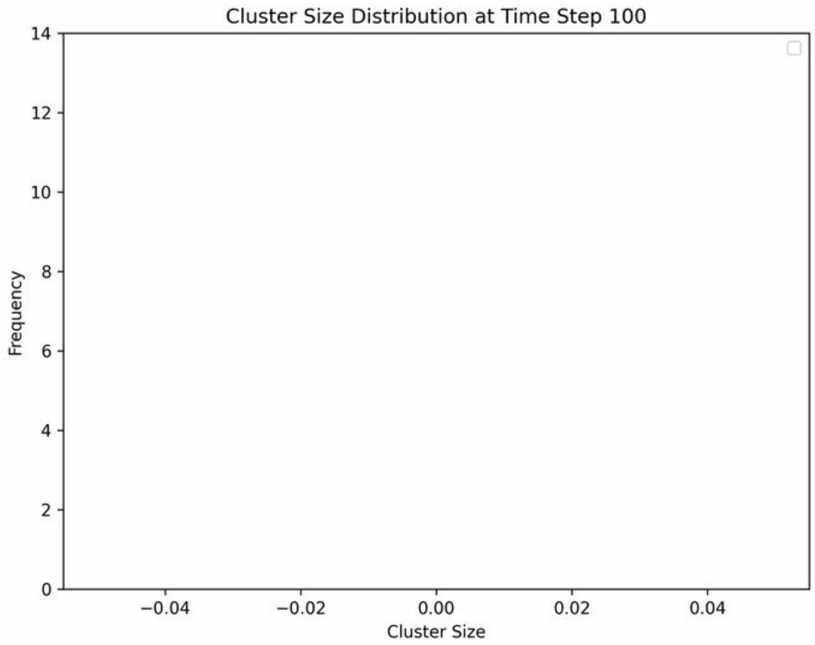


Vessels in tumor area at breakpoint



Is the tumor clusters' power law distribution influenced by the same distribution in the vessels?

Vessel Growth:
clustering behavior over time

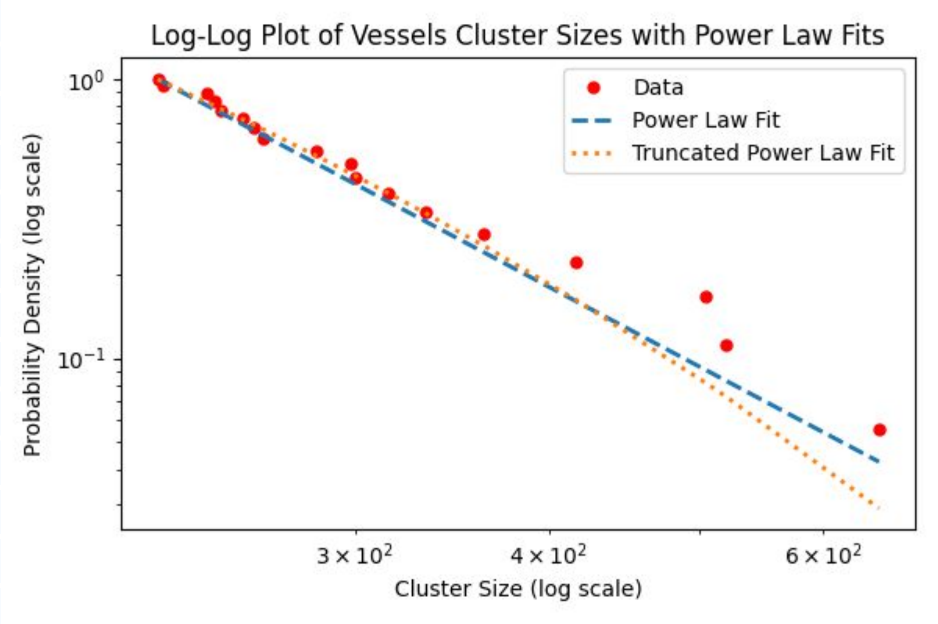


- ➔ 100 simulations.
- ➔ 10 combined datasets per simulation.

```
Proportion of Power Law: 0.00%
Proportion of Truncated Power Law: 0.00%
```

Vessel cluster sizes do not follow a power law distribution around the tumor.

Vessel Growth:
clustering behavior over time

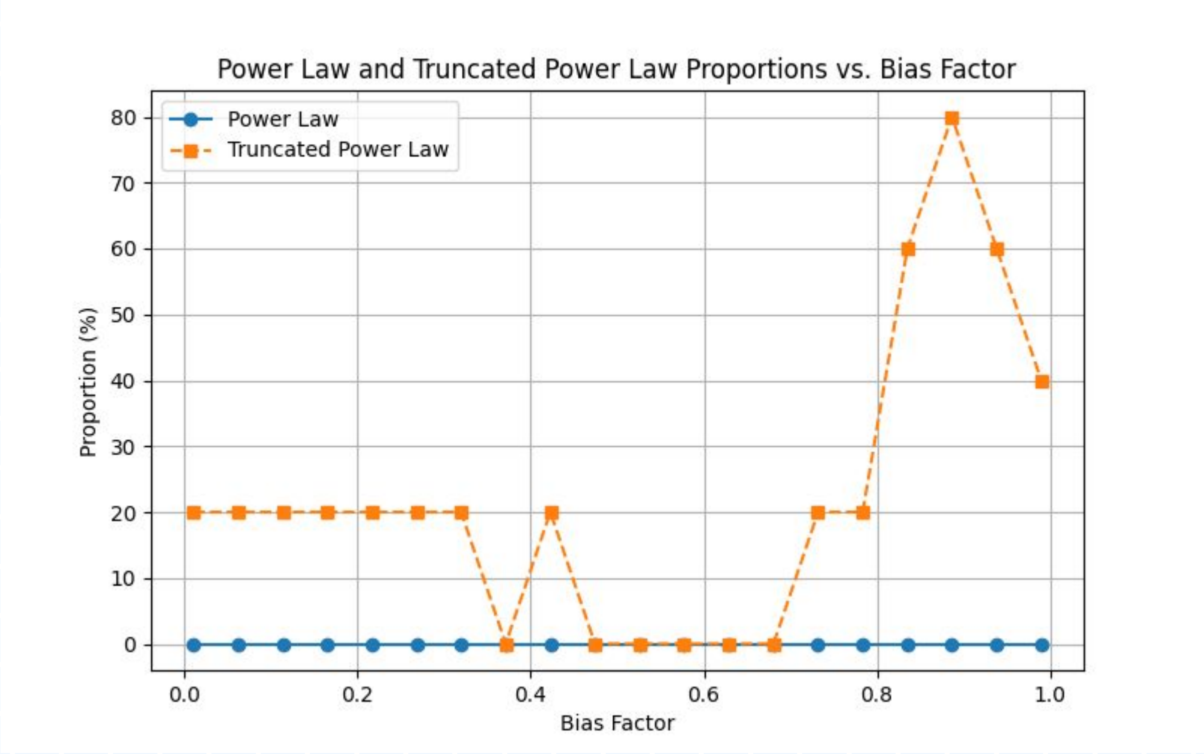


Example of vessel cluster sizes fit. All p-values >> 0.05.

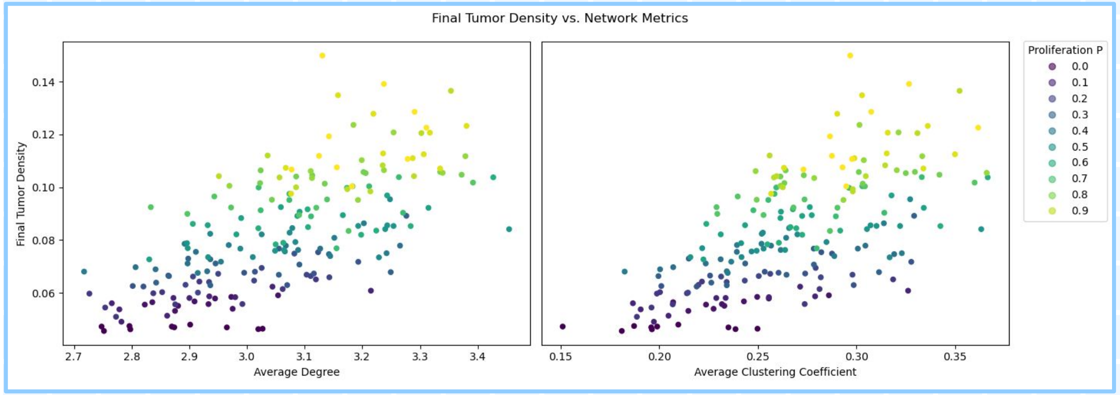
Power law VS	R	p-value
Exponential	0.04	0.97
Lognormal	-0.35	0.73
Truncated power law	-0.47	0.55

Truncated Power law VS	R	p-value
Exponential	0.45	0.65
Lognormal	0.89	0.37
Power law	0.47	0.55

Bias Factor and Tumor Clusters



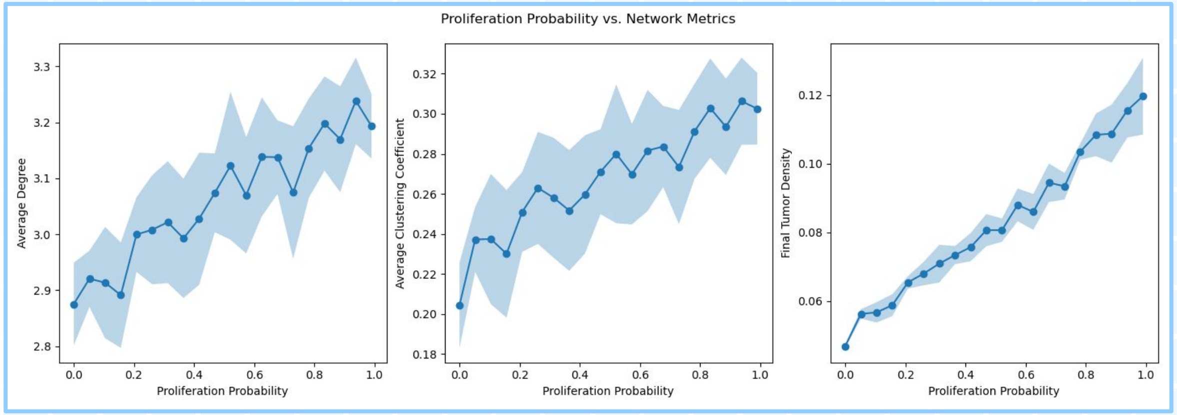
Thank you!

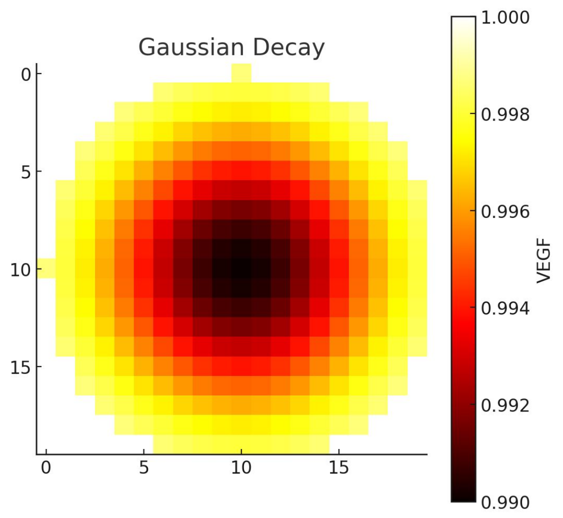


Appendix 1

Varying the probability of tumor cell growth/death

Proliferation Probability VS Network Metrics





Gaussian Decay of VEGF due to Vessel Growth

$$VEGF(x,y) = \max\left(0, VEGF(x,y) \times (1 - w(d) \times (1 - \text{decay\_factor}))\right)$$

$$w(d) = e^{-\frac{d^2}{2\sigma^2}}$$

decay_factor = 0.99

$$\sigma = 10/2, \qquad d = 10$$