

SUPPORTING INFORMATION

In-silico Dynamic Analysis of Cytotoxic Drug Administration to Solid Tumours: Effect of Binding Affinity and Vessel Permeability

Vasileios Vavourakis, Triantafyllos Stylianopoulos, Peter A. Wijeratne

Vascular network model parameters

List of model parameters associated with the *Vascular Network Module* (see Fig 1). Parameters with a star (*) correspond to non-perfused or hypo-perfused vessels, while those with a dagger (†) correspond to well-perfused vessels. The parameters with a double dagger (‡) denote the pre-set parameter values of the original vascular network, while the cell marked with an asterisk denotes shared value for both tissue types.

Parameter	Description	Host	Tumour	Source
k_T [m]	chemotaxis in angiogenesis	1.		[1]
k_ϵ [m]	haptotaxis in angiogenesis	0.3		[1]
k_m [Pa ⁻¹]	mechanotaxis in angiogenesis	0.01		[1]
\tilde{R} [μm]	see Eq (16) in [1]	4.		[2]
v_{v-0}, v_{v-1} [$\mu\text{m d}^{-1}$]	see Eq (16) in [1]	5.5, 479.7		[2]
$v_{v-\max}$ [$\mu\text{m d}^{-1}$]		250.		[1, 2]
τ^* [-]	TAF threshold above which angiogenesis occurs	0.01		[1]
μ_D, σ_D [μm]	median and standard deviation of distance-related probability function P_D	$150. \pm 15^*, 300. \pm 30^\dagger$		[1]
μ_A, σ_A [d]	median and standard deviation of age-related probability function P_A	$0.5 \pm 0.25^*, 1.25 \pm 0.25^\dagger$		[1]
[μm]	minimum distance (between two different branches) to enforce anastomosis	40.		[1]
R [μm]	capillary lumen radius of original (host) vessels; range of R for tumour vessels	$80.^{\ddagger}; 5.-60.$		[3, 4]
h [μm]	capillary wall thickness of original vessels; range of h for tumour vessels	$5.5^{\ddagger}; 3.-5.$		[3, 4]
r_p [nm]	capillary wall pore size of original vessels; average value of r_p for tumour vessels	$1.^{\ddagger}; [10., 50., 150.]$		[5, 6]
γ_p [-]	fraction of endothelium surface occupied by pores for original vessels; value of γ_p for tumour vessels	$1.e-4^\dagger; 10.e-4$		[7]

References

1. Vavourakis V, Wijeratne PA, Shipley R, Loizidou M, Stylianopoulos T, Hawkes DJ. A Validated Multiscale In-Silico Model for Mechano-sensitive Tumour Angiogenesis and Growth. PLOS Computational Biology. 2017;13(1):e1005259. doi:10.1371/journal.pcbi.1005259.

-
2. Wood LB, Ge R, Kamm RD, Asada HH. Nascent vessel elongation rate is inversely related to diameter in in vitro angiogenesis. *Integrative Biology*. 2012;4:3579–3600.
 3. Hashizume H, Baluk P, Morikawa S, McLean JW, Thurston G, Roberge S, et al. Openings between Defective Endothelial Cells Explain Tumor Vessel Leakiness. *The American Journal of Pathology*. 2000;156(4):1363–1380. doi:10.1016/S0002-9440(10)65006-7.
 4. Morikawa S, Baluk P, Kaidoh T, Haskell A, Jain RK, McDonald DM. Abnormalities in Pericytes on Blood Vessels and Endothelial Sprouts in Tumors. *The American Journal of Pathology*. 2002;160(3):985–1000. doi:10.1016/S0002-9440(10)64920-6.
 5. Sarin H. Physiologic upper limits of pore size of different blood capillary types and another perspective on the dual pore theory of microvascular permeability. *Journal of Angiogenesis Research*. 2010;2(1):1–19. doi:10.1186/2040-2384-2-14.
 6. Chauhan VP, Stylianopoulos T, Martin JD, Popovic Z, Chen O, Kamoun WS, et al. Normalization of tumour blood vessels improves the delivery of nanomedicines in a size-dependent manner. *Nature Nanotechnology*. 2012;7(6):383–388. doi:10.1038/nnano.2012.45.
 7. Jain RK, Tong RT, Munn LL. Effect of vascular normalization by antiangiogenic therapy on interstitial hypertension, peritumor edema, and lymphatic metastasis: Insights from a mathematical model. *Cancer Research*. 2007;67(6):2729–2735. doi:10.1158/0008-5472.CAN-06-4102.