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Biochemomechanical poroelastic theory of avascular tumor growth

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ABSTRACT

Tumor growth is a complex process involving genetic mutations, biochemical regulations, and mechanical deformations. In this paper, a thermodynamics-based nonlinear poroelastic theory is established to model the coupling among the mechanical, chemical, and biological mechanisms governing avascular tumor growth. A volumetric growth law accounting for mechano-chemo-biological coupled effects is proposed to describe the development of solid tumors. The regulating roles of stresses and nutrient transport in the tumor growth are revealed under different environmental constraints. We show that the mechano-chemo-biological coupling triggers anisotropic and heterogeneous growth, leading to the formation of layered structures in a growing tumor. There exists a steady state in which tumor growth is balanced by resorption. The influence of external confinements on tumor growth is also examined. A phase diagram is constructed to illustrate how the elastic modulus and thickness of the confinements jointly dictate the steady state of tumor volume. Qualitative and quantitative agreements with experimental observations indicate the developed model is capable of capturing the essential features of avascular tumor growth in various environments.

1. Introduction

Solid tumors account for more than 85% of cancer mortality (Jain, 2005). Examples of solid tumors include sarcomas, carcinomas, and lymphomas, which often originate from the transformation of small nodes of normal cells into tumor cells that either lose or cease to respond to normal physiological regulations (Hanahan and Weinberg, 2000; Radisky et al., 2001). The development of solid tumors is a biological process involving multifactorial determinants, e.g. cell molecular and genetic abnormalities, cell–cell and cell–extracellular matrix (ECM) interactions, and the supply of oxygen and nutrients (Hanahan and Weinberg, 2000; Tracqui, 2009).

It has been recognized that, besides genetic alterations and biochemical factors, mechanical cues sensed by or transduced to tumor cells also play a vital role in the expansion, invasion, and metastasis of tumors (Jain et al., 2014). The mechanical

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Nomenclature

Deformation

$\mathbf{A}(\lambda_i)$	Elastic deformation tensor (and its principal components)
$\mathbf{G}(g_i)$	Growth tensor (and its principal components)
$\mathbf{F}$	Deformation gradient tensor
$\mathbf{C}$	Right Cauchy-Green tensor
$\mathbf{I}$	Second-order unit tensor
ρ_0, ρ	Mass densities at the reference state and the current state
J, J_A, J_G	Volumetric ratios of deformation, elastic deformation and growth
Γ	Mass production rate
$\mathbf{L}_G$	Growth rate tensor
ϕ_L	Lagrangian porosity
$\phi_E(\phi_E^0)$	Eulerian porosity (and its initial value)

Fluid constituent

m_α	Mass of fluid constituent α
ρ_α	Mass density of fluid constituent α
ξ_α	Consumption rate of fluid constituent α
$\mathbf{Q}_\alpha$, $\mathbf{q}_\alpha$	Mass fluxes of fluid constituent α
$\mathbf{v}_{\alpha s}$, $\mathbf{v}_{\alpha\beta}$	Relative velocities of fluid constituents
$h_{\alpha s}$, $h_{\alpha\beta}$	Diffusive drag coefficients of fluid constituents
$c_\alpha^g(c_0^g)$	Concentration of fluid constituent α in the tumor (minimal nutrient concentration required for cancer cell survival)
$c_\alpha(c_0)$	Concentration of fluid constituent α in the solvent (initial nutrient concentration)
$\mathbf{v}$, $\mathbf{v}_h$	Velocity vectors of the tumor and the incoming solid mass

Force

$\mathbf{b}$	Total stress driving tumor growth
$\mathbf{b}_H(b_H)$	Homeostatic stress tensor (and its principal component)
$\mathbf{b}_{Eshelby}$	Eshelby stress tensor
$\mathbf{P}$	First Piola-Kirchhoff stress tensor
P	External pressure
p (p_0)	Fluid pressure (and its initial value)
$\boldsymbol{\sigma}(\sigma_i)$	Cauchy stress tensor (and its principal components)
$\bar{\sigma}$	Mean Cauchy stress
$\mathbf{f}$	Body force per unit mass
$\mathbf{t}$	Surface traction
$\mathbf{n}$	Unit outward normal vector in the current configuration

Energy

P_{int}, P_{ext}	Internal and external mechanical work rates
K	Kinetic energy per unit volume in the reference configuration
E, E_h	Internal energies of the tumor and the incoming solid mass per unit volume in the reference configuration
e_α	Internal energy density of fluid constituent α per unit mass
η, η_h	Entropies of the tumor and the incoming solid mass
η_α	Entropy of fluid constituent α per unit mass
χ_α	Enthalpy of fluid constituent α per unit mass
ψ, ψ_h	Helmholtz free energy densities of the tumor and the incoming solid
ω_α	Gibbs free energy (i.e. chemical potential) of fluid constituent α per unit mass
$\psi_s(W_0)$	Free energy of the solid skeleton per unit volume in the reference configuration
W, W_h	Free energies of the solid skeleton and the incoming solid mass per unit volume in the intermediate configuration
W_s, W_p	Free energies of the drained solid skeleton and the saturated pores
W_m	Free energy of the elastic matrix

Geometry of tumor spheroid

R, r	Radial positions of the tumor spheroid in the reference and the current configurations
R_0	Initial radius of the tumor spheroid in the reference configuration
R_n	Radius of the necrotic core of the tumor spheroid in the reference configuration
v	Average growth velocity of the tumor spheroid
A_0	Surface area of the tumor spheroid in the reference configuration

Physical property

μ	Shear modulus of the tumor
μ_m	Shear modulus of the elastic matrix
H_m	Thickness of the elastic matrix
Ω	Biot modulus
B	Biot coefficient
K^g	Constant in growth law
ϑ,γ	Constants in nutrient consumption
D,D^0	Nutrient diffusivities in the tumor and free solution
$k(k_{ref})$	Permeability of the tumor (and its reference value)
R_{gas}	Gas constant
Θ	Temperature