Available online at www.sciencedirect.com
SCIENCE DIRECT®
PERGAMON
International Journal of Heat and Mass Transfer 46 (2003) 4989–5003
International Journal of HEAT and MASS TRANSFER
www.elsevier.com/locate/ijhmt

Review

The role of porous media in modeling flow and heat transfer in biological tissues

A.-R.A. Khaled [a], K. Vafai [b,*]

[a] Department of Mechanical Engineering, The Ohio State University, Columbus, OH 43210, USA
[b] Department of Mechanical Engineering, University of California, A363 Bourns Hall, Riverside, CA 92521-0425, USA

Received 11 March 2003; received in revised form 16 May 2003

Abstract

Flow and heat transfer in biological tissues are analyzed in this investigation. Pertinent works are reviewed in order to show how transport theories in porous media advance the progress in biology. The main concepts studied in this review are transport in porous media using mass diffusion and different convective flow models such as Darcy and the Brinkman models. Energy transport in tissues is also analyzed. Progress in development of the bioheat equation (heat transfer equation in biological tissues) and evaluation of the applications associated with the bioheat equation are analyzed. Prominent examples of diffusive applications and momentum transport by convection are discussed in this work. The theory of porous media for heat transfer in biological tissues is found to be most appropriate since it contains fewer assumptions as compared to different bioheat models. A concept that is related to flow instabilities caused by swimming of microorganisms is also discussed. This concept named bioconvection is different from blood convection inside vessels. The works that consider the possibility of reducing these flow instabilities using porous media are reviewed.

Contents

* Corresponding author. Tel.: +1-909-787-2135; fax: +1-909-787-2899.
E-mail address: vafai@engr.ucr.edu (K. Vafai).

0017-9310/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0017-9310(03)00301-6

1. Introduction

Porous medium is defined as a material volume consisting of solid matrix with an interconnected void. It is mainly characterized by its porosity, ratio of the void space to the total volume of the medium. Earlier studies in flow in porous media have revealed the Darcy law [1] which relates linearly the flow velocity to the pressure gradient across the porous medium. The porous medium is also characterized by its permeability which is a measure of the flow conductivity in the porous medium. An important characteristic for the combination of the fluid and the porous medium is the tortuosity which represents the hindrance to flow diffusion imposed by local boundaries or local viscosity. The tortuosity is especially important as related to medical applications. Later developments in porous media led to extended advanced models for the Darcy law such as Forchheimer's equation [2] and Brinkman's equation [3] where the former is applicable for large flow velocities while the latter takes into account the boundary effects. These effects are not taken into account in the Darcy's equation.

Heat transfer in human tissues involves complicated processes such as heat conduction in tissues, heat transfer due to perfusion of the arterial-venous blood through the pores of the tissue (blood convection), metabolic heat generation and external interactions such as electromagnetic radiation emitted from cell phones. Bioheat is usually referred to heat transfer in the human body. Biomedical engineers have attempted to accurately model bioheat transfer in tissues since they are the basis for the human thermotherapy [4] and the human thermoregulation system [5].

The development of transport models in porous media had a bearing in the progress of several applications such as geology, chemical reactors, drying and liquid composite molding, combustion and biological applications. In this review, the impact of the theory of transport in porous media on medical and biological sciences is discussed for different applications.

The review is arranged into five important categories in biological applications. The first one deals with transport in porous tissues due to mass diffusion. The second topic deals with different investigations in convective transport applications in biological tissues. Next, approaches in obtaining structural information from biological media such as magnetic resonance imaging (MRI) relevant to porous media are discussed. The fourth area that is covered is the development of the bioheat equation within the tissue and the incorporation of the theory of porous medium. The principle of bioconvection is explained and ways to reduce flow instabilities in bioconvection using porous media models are discussed. These topics are reviewed and available models using porous media are synthesized and analyzed for future works. In this review, only works which are most pertinent to the outlined study are selected and analyzed. These works involve the following applications: tissue generation in scaffolds, transport in brain tissues, MRI applications in analyzing the structure of porous media, liquid chromatography, transport of macromolecules in aortic media, blood flow through contracting muscles, interstitial fluid flow in axisymmetric soft connective tissue, thermal simulations within the brain after head injury, hyperthermic sessions, heat transfer in muscle and skin tissues, thermal therapy applications and others.

2. Mass diffusion in tissues

Tissues can be treated as a porous medium as it is composed of dispersed cells separated by connective voids which allow for flow of nutrients, minerals, etc. to reach all cells within the tissue (Fig. 1). Mass transports of these substances in many biological and medical applications are achieved by diffusion within the tissue. These applications can be found mainly in tissue regeneration using scaffolds, transport of drugs and nutrients to brain cells and the transport of residual solvents in scaffolds which are used in fabricating the biodegradable scaffolds.

2.1. Mass diffusion in tissue regeneration applications

Galban and Locke [6,7] present an interesting theoretical work that considers mass diffusion as the only

Nomenclature

C	concentration of a species
C_σ	concentration of a species in the cell phase
c_p	tissue specific heat
c_{p_b}	blood specific heat
D	diffusivity of the pure fluid
D^*	effective diffusivity of the porous medium
h_{bs}	interstitial convective heat transfer coefficient
K	permeability of the porous medium
K_s	saturation constant
K_c	modified saturation constant
K_m	Michele–Menten constant
k	tissue thermal conductivity
k_b	blood thermal conductivity
k_d	death rate coefficient
n	semiempirical parameter
P	fluid pressure
q_m	heat generation within the tissue
R_σ	localized rate of cell growth
$\bar{r}$	dimensional radial coordinate
r_σ	radius of the cell phase
T	tissue temperature
$\langle T\rangle^b$	local arterial blood averaged temperature
$\langle T\rangle^s$	local tissue averaged temperature
T_B	arterial blood temperature
t	time
u	Darcy velocity
u_b	blood velocity
$\bar{u}$	dimensional axial velocity
$\mathbf{V}$	velocity vector
V	averaging volume
V_{max}	rate constant
V_σ	volume of the solid phase
$\mathbf{v}$	Darcy velocity vector
W_b	blood volumetric perfusion rate
x	x-coordinate

Greek symbols

δ	average distance between the transverse blood vessels
ε	porosity of the porous medium
λ	tortuosity
ρ	tissue density
ρ_f	fluid density
ρ_σ	density of the cell phase
μ	dynamic viscosity of the pure fluid
μ_∞	Casson's viscosity
$\tilde{\mu}$	effective viscosity of the porous medium
τ_y	fluid yield stress
$\bar{\tau}$	fluid shear stress

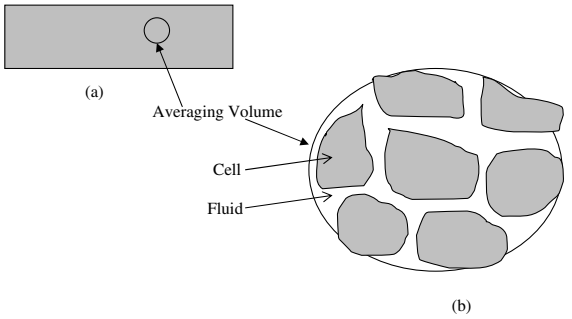

Fig. 1. Schematic diagram for a tissue: (a) tissue and (b) averaging volume.

mechanism for cell seeding and nutrient transport in a scaffold. They developed mathematical models for chondrocyte generation (mature cartilage cells that serve as an early skeletal frame work, they are more flexible and compressible than bone) and nutrient consumption in order to analyze the behavior of cell growth in a biodegradable polymer matrix. Galban and Locke [7] related mathematically in their model the increase in the cell mass in the polymer matrix to the transport of the nutrients. They considered applications where the transport of nutrients is by diffusion such as for static culture conditions. Accordingly, they described reaction and diffusion of nutrients in a porous scaffold using the primary species continuity equations along with the volume averaging method, a well established method in porous media [8]. The volume averaging method was employed in their work in order to obtain a single averaged nutrient continuity equation which contains the effective transport properties such as the effective diffusion and rate coefficients. These properties were related to the porosity of the scaffold. The volume fraction of the cells which is related to porosity of the scaffold is determined by a mass balance on the seeded cells. Their finding for the tissue growth rate is summarized by the following equation:

$$\frac{d\varepsilon_\sigma}{dt} = \frac{1}{\rho_\sigma V}\int_{V_\sigma} R_\sigma \, dV \tag{1}$$

where ε_σ is the ratio of the volume of the cell phase within the averaging volume in the scaffold to the averaging volume. V_σ is the volume of the cell phase in the scaffold within the averaging volume. The parameters R_σ and ρ_σ are the localized rate of cell growth and the

Table 1
Different kinetic models for the growth rate

Kinetic models	Governing equation
Modified contois	$R_\sigma = \left[\frac{k_g C_\sigma^n}{K_c \rho + C_\sigma^n} - k_d\right]\rho_\sigma$
Moser	$R_\sigma = \left[\frac{k_g C_\sigma^n}{K_s + C_\sigma^n} - k_d\right]\rho_\sigma$
nth order heterogeneous	$R_\sigma = k_h C_\sigma^n\|_{r_\sigma}$

specific cell density, respectively. Galban and Locke [7] listed three growth kinetics presented in the literature which correspond to three different mechanisms. These are the modified Contois, Moser and an nth-order heterogeneous reaction at the cell–void interface within the implant. Their mathematical model is summarized in Table 1. In Table 1, k_g is the homogenous growth rate coefficient while k_h is the heterogonous growth rate coefficient. The parameters C_σ, K_c, K_s, ρ, k_d, r_σ and n are the concentration of the nutrient within the cell phase, modified Contois saturation constant, saturation constant, the overall cell density, the death rate coefficient, the radius of cell phase in the averaging volume within the scaffold and a semiempirical parameter named as the Moser parameter, respectively. They compared the theoretical cell growth data utilizing the previous models with the experimental data found in the literature. The results of comparisons indicated that cellular functions along with mass transfer processes in porous media can illustrate to a degree the general trends in the cell growth behavior for various scaffold thicknesses. However, additional experimental data and model improvements are required to accurately explain the process of cell growth.

2.2. Mass diffusion in brain tissues

Nicholson [9] in his report about diffusion in brain tissues indicated that diffusion is an essential mechanism for delivering glucose and oxygen from the vascular system to brain cells as well as in delivering drugs to the brain and in the transport of informational substances between cells, a process known as volume transmission. He pointed that diffusion-generated concentration distributions of well-chosen molecules in the brain tissue reveal its structure. This structure is characterized by the volume fraction (porosity) of the tissue and the tortuosity. Nicholson [9] demonstrated that an increase in the tortuosity and a decrease in the porosity have significant effects in reducing the effective mass diffusivities of species. He derived the following equation for mass transport due to diffusion for isotropic tissues:

$$\frac{\partial C}{\partial t} = D^*\nabla^2 C + \frac{s}{\varepsilon} \tag{2}$$

where C, D^*, s, ε and t are the volume average concentration of the species, effective diffusivity, mass source density, porosity of the tissue and time, respectively. As shown in the work of Nicholson [9], the effective diffusivity is related to the tortuosity of the tissue λ and the diffusivity in the absence of the porous medium through the following relation:

$$D^* = \frac{D}{\lambda^2} \tag{3}$$

El-Kareh et al. [10] introduced additional viscosity function f_η into the definition of the effective diffusivity as shown in Eq. (4)

$$D^* = \frac{D}{(\lambda f_\eta)^2} \tag{4}$$

Nicholson [9] also incorporated several kinetics models in the mass diffusion equation such as the nonlinear Michele–Menten (MM) kinetics [11]. This kinetic model can describe the entry and consumption of oxygen by cells as it diffuses and the removal of transmitter substances, e.g. dopamine (neurotransmitter and hormone), from extracelluar cells. Eq. (2) is changed to the following when MM kinetics exists

$$\frac{\partial C}{\partial t} = D^*\nabla^2 C + \frac{s}{\varepsilon} - \frac{V_{max} C}{\varepsilon(K_m + C)} \tag{5}$$

where V_{max} is a rate constant which represents a measure of the number of uptake sites. It is worth noting that uptake means the absorption by a tissue of some substance, food material, mineral and others. The MM constant K_m is a measure of the dissociation constant for binding of the substrate, e.g. dopamine, to the uptake sites on the cell membrane.

An example for the reduction in the protein diffusivity due to tortuosity is shown in the work of Whang et al. [12]. Nicholson and Rice [13] implied that the tortuosity in brain tissue increases with a decrease in the porosity. Nicholson [9] included the general diffusion equation to be applied for anisotropic tissues such as brain tissues. This is summarized in the following equation in Cartesian coordinates:

$$\frac{\partial C}{\partial t} = \frac{D}{\lambda_x^2}\frac{\partial^2 C}{\partial x^2} + \frac{D}{\lambda_y^2}\frac{\partial^2 C}{\partial y^2} + \frac{D}{\lambda_z^2}\frac{\partial^2 C}{\partial z^2} + \frac{s}{\varepsilon} \tag{6}$$

where λ_x, λ_y and λ_z are the three off-diagonal components of the tortuosity tensor. In addition, he pointed that void fraction and tortuosity can reveal how the local geometry of the brain changes with time or under pathological conditions. Additional examples that focus on transport of fluids by diffusion inside porous tissues can be seen in the works of Woerly et al. [14] and Koegler et al. [15]. They first analyzed neural tissue formations within porous hydrogel while discussing the feasibility of using liquid CO for reducing residual solvents that are used in fabricating biodegradable polymeric devices (scaffolds). Reduction of residual solvents

is important since excess solvent can interfere with tissue response and alter the mechanical properties of the scaffold. They fitted their results to the simple diffusion model and predicted the time needed to dry different scaffold sizes.

3. Magnetic resonance imaging applications in porous media

Biological tissues contain fluid-filled compartments (e.g. cells) that restrict the movement of the bulk solvent water whose molecules move on a variety of time scales including random Brownian diffusion and interact with macromolecules within the tissues. This can affect their nuclear magnetic resonance, an imaging technique that does not use radiation) relaxation rates. Gore et al. [16] indicated that technical developments that have been driven on by biomedical applications of MRI can be utilized in characterizing porous media. Gore et al. [16] referred to some studies in their lab that include the development of multiple quantum coherent methods for studies of water diffusion in anisotropic macromolecular assemblies and multiple selective inversion imaging to depict the ratios of proton pool sizes and rates of magnetization transfer between proton populations as well as the diffusion tensor imaging to illustrate tissue anisotropies. These show how various approaches utilized in obtaining structural information from biological media are also applicable to porous media.

4. Flow convection in biological tissues

In certain biomedical applications, diffusion may not be a sufficient mechanism for mass transport in porous structures. The following applications illustrate the necessity for convective transport models in biological systems with porous structures. The first application is related to the production of an osteoinductive device (material for repair of bone defects). This can be achieved by the culture of seeded osteoblastic cells in three-dimensional osteoconductive scaffolds in vitro. However, it is a challenge for tissue engineers to culture cells in scaffolds sufficiently large to bridge critical-sized defects. This is because diffusion may not be sufficient to supply nutrients into large scaffolds causing cells to grow preferentially at the periphery under static culture conditions. Goldstein et al. [17] considered three alternative culturing schemes that convect media: a spinner flask, a rotary vessel, and a perfusion flow system (direct pouring of nutrient and cell flows, Fig. 2). They found that cell numbers per foam to be similar with all culturing schemes indicating that cell growth could not be enhanced by convection, but histological analysis (cell analysis) indicates that the rotary vessel and perfusion

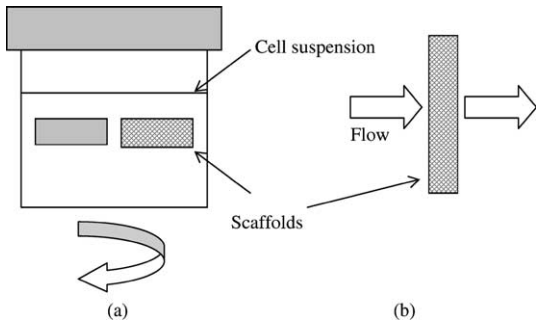

Fig. 2. Two culturing media: (a) spinner flask and (b) perfusion flow system.

flow system produced a more uniform distribution of cells throughout the foams consequently a more uniform porosity for the scaffold. They concluded that culturing techniques that utilize flow perfusion systems improve the properties of the seeded cells over those maintained in static culture.

The second application is related to adsorptive separation by high performance liquid chromatography (separation based on differential absorption). This is an important process in biotechnology for separation of proteins where one of its important aspects is the packing material. It is composed of porous particles and it has been continuously improved in order to reduce intraparticle mass transfer resistances. Leitao et al. [18] indicated that elution chromatography (the separation, by washing, of one solid from another) experiments show that mass transfer resistance inside bidisperse porous particles, Fig. 3 (contains microporous region made by spherical microparticles and macroporous region made by interconnected throughpores) is substantially reduced by intraparticle convection. They performed a mathematical and experimental study on separations of two proteins, myoglobin (found in red skeletal muscle) and bovine serum albumin (found in blood and lymph) using bidisperse porous medium. In their mathematical model, they accounted for adsorption on throughpore walls, on the surface as well as in the interior of microparticles of the bidisperse particles and intraparticle convection in throughpores where they utilized the

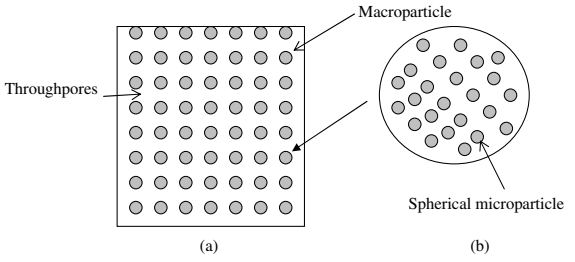

Fig. 3. Schematic diagram of bed with bidisperse particles: (a) bidisperse medium and (b) macroparticle.

Darcy model to govern the flow in the throughpores. They found that protein transport is strongly restricted by a film resistance around microparticles and that experimental convection effects on porous particles are higher than those predicted by the mathematical model. They attributed this anomaly to a flow rate dependent film resistance around microparticles.

Another application is illustrated in the work of Kim and Tarbell [19] who combined a simple mechanohydraulic model based on a two parameter strain-dependent permeability function developed by Klanchar and Tarbell [20], with a pore theory in order to determine the transport properties of macromolecules in an artery wall deformed inhomogeneously by the transmural (through a wall) pressure. They determined the spatial distribution of the porosity, solute partition, pore radius and the macromolecular solute concentration in the media based on the combined theory and they found out their relationships with the transmural pressure. The predictions from the pore theory were found to be in good agreement with experimental measurements. Their results indicate that convection is the dominate mechanism over diffusion for albumin transport through the aortic media. Also, the results demonstrated that the transport properties of planar tissues that are used in vitro experiments can be different from those of intact vessels in their natural cylindrical configuration. This is ascribed to the variation in tissue deformation of these vessels in their natural configuration.

4.1. Applications of Darcy model to flow in biological tissues

Darcy model is considered to be the earliest flow transport model in porous media. In his experiments on unidirectional flow in a uniform medium, Henry Darcy [1] revealed a linear proportionality between the flow velocity and the applied pressure difference. Darcy model is expressed by:

$$u = -\frac{K}{\mu}\frac{\partial P}{\partial x} \tag{7}$$

where u, P, μ and K are the Darcy velocity (the average of the fluid velocity over the cross section), fluid pressure, dynamic viscosity of the fluid and the permeability of the porous medium, respectively. The permeability K of the medium which has dimension of $(\text{length})^2$ depends only on the geometry of the medium. In three dimensions, Eq. (7) can be generalized to

$$\mathbf{v} = \mu^{-1}\mathbf{K}.\nabla P \tag{8}$$

where the permeability $\mathbf{K}$ is a general second-order tensor. The terms $\mathbf{v}$ and ∇P are Darcy velocity and pressure gradient vectors. For isotropic porous medium, the permeability is scalar and Eq. (8) reduces to

$$\nabla P = -\frac{\mu}{K}\mathbf{v} \tag{9}$$

Darcy model has been utilized successfully in several biomedical applications leading to a number of developments in these areas. Huyghe and Vancampen [21] presented a constitutive formulation for finite deformation of porous solids in order to model flow through different hierarchical arrangements. They developed an extended Darcy model utilizing an averaging method which transformed the network of pores into a continuum. They considered the pores as a network of cylindrical vessels in which Poiseuille-type pressure-flow relationships are valid. The relationships between stress, strain, strain rate, fluid volume fraction, fluid volume fraction rate and time were obtained using irreversible thermodynamics arguments. Their work has applications in the field of the mechanics of blood perfused through soft tissues. They demonstrated that their theory is consistent with Biot's finite deformation theory in porous media for the limiting case where the pore structure has no hierarchy. It is worth noting that Biot's theory is considered the first developed theory that can be used to analyze the linear elastic behavior of a porous medium. Later, Vankan et al. [22] compared a hierarchical mixture model of blood perfused biological tissue that utilizes an extended Darcy equation for blood flow with a network analysis of the biological tissue. Good correspondence is achieved between both methods if the hierarchical quantification is based on the network fluid pressure.

Vankan et al. [23] also performed a simulation for blood flow through a contracting muscle, with a hierarchical structure of pores (the hierarchy corresponds to the tree-like vascular structure). The fluid flow was described by a Darcy model for deformable porous media with second-order permeability tensor while fluid pressure and hydrostatic solid pressures were related through an elastic fluid solid interface. The state of the fluid, the Darcy permeability tensor and the elastic interface were taken to be functions of space as well as the hierarchical level. They found that their calculated blood pressures were approximately corresponding to blood pressures measured in skeletal muscles.

Butler et al. [24] studied interstitial fluid flow in axisymmetric soft connective tissues such as ligaments or tendons (fibrous tissue connecting bones and cartilage and connective tissue that connects muscle to bone, respectively) when they are in tension. The flow in these tissues were modeled as Darcian flow through a porous medium having the pressure and the velocity of the interstitial fluid as the unknown variables. A parametric study was conducted by varying the fluid viscosity and the permeability of the solid matrix where they were found to strongly affect the resulting fluid flow behavior. Further, computed levels of fluid flow predicted a possible mechanism for load transduction for cells in the tissue.

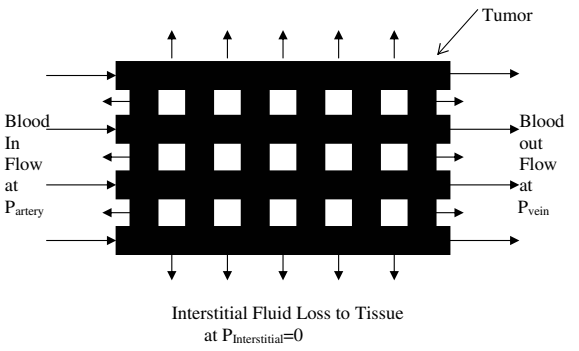

Fig. 4. A model for the transport through a tumor; arrangements of vessels in parallel layers, blood is supplied at P_{artery} and removed at P_{vein}, the interstitial pressure in the surrounding normal tissue satisfies $P_{interstitial} = 0$.

An important domain that deals with the application of the Darcy model to flow through tissues is the blood flow in tumors (abnormal mass of tissue that results from excessive cell division that is uncontrolled and progressive). Tumor blood flow is highly heterogeneous when compared to normal tissues. Therefore, the growth of the tumor and its response to therapy are determined by transport of diffusible drugs to cancer cells and consequently by their blood supply. The high leakiness of tumor vessels could enhance fluid exchange between the vascular and interstitial fluid flow which could lead to a coupling between vascular, transvascular, and interstitial fluid flow as shown in Fig. 4. Baish et al. [25] considered a simple network model to model the important features of flow through a network of permeable and compliant vessels embedded in an isotropic porous medium. They used the Darcy model to represent the flow through the porous medium and the Starling law to describe the vascular fluid exchange (assuming vascular fluid exchange flow rate is proportional to the pressure difference across the vascular–porous medium interface), and the leakiness from the vessels. Their results show that drug delivery for chemotherapy and oxygenation that are needed for radiotherapy may face difficulty to reach the central region of the tumor despite the fact that highly permeable vessels are present in these regions.

Lei et al. [26] developed a complex model for transvascular exchange and extravascular transport of both fluid and macromolecules in a spherical solid tumor. The microvascular lymphatics and tissue space were each considered as a porous medium. The flow of blood and lymph were described by the Darcy model while the interstitial fluid is assumed to obey the Starling's law. They obtained analytical solutions for an isolated tumor as well as for the normal tissue surrounding the tumor. Their calculated interstitial pressures agreed with the experimental observations. Their results and the results of Milosevic et al. [27] revealed that the elevated interstitial pressure was a major barrier in the penetration of macromolecular drug into a tumor.

Preziosi and Farina [28] analyzed flow of a Newtonian fluid in a porous medium in the presence of mass exchange between the constituents. They found out that the Darcy model needs to be modified to account for the mass exchange. Their study was based on a thermodynamical analysis and using symmetry and frame indifferent arguments. Preziosi and Farina [28] results have application in tissue regeneration using scaffolds under convective conditions where the correction coefficient for the Darcy model is proportional to the cell growth rate.

4.2. Applications of the Brinkman model to flows in biological tissues

Darcy model ignores the boundary effects on the flow. This assumption is not valid when the boundaries of the porous medium have to be accounted for. As such, the Brinkman model is usually employed

$$\nabla P = -\frac{\mu}{K}\mathbf{v} + \tilde{\mu}\nabla^2\mathbf{v} \tag{10}$$

Eq. (10) is referred in the literature as the Brinkman model and was first developed by Brinkman [3,29]. The first viscous term on the right is the Darcy term while the second term on the right is analogous to the momentum diffusion term in the Navier–Stokes equation with $\tilde{\mu}$ being the effective dynamic viscosity of the medium. For isotropic porous medium, Bear and Bachmat [30] argued that the effective viscosity is related to the porosity through the following relation:

$$\frac{\tilde{\mu}}{\mu} = \frac{1}{\varepsilon}\lambda^* \tag{11}$$

where ε and λ^* are the porosity and tortuosity of the medium, respectively. It is worth noting that the tortuosity is also a function of the porosity and can be represented by $\lambda^* = \sqrt{\varepsilon}$ for packed beds [31].

Brinkman model has been effectively utilized in several biomedical research works. Dash et al. [32] employed the Brinkman equation to model the pathological blood flow as accumulations of fatty plaques of cholesterol and artery-clogging blood clots increase in the lumen (the cavity or channel within a tube) of the coronary artery shown in Fig. 5. They considered the clogged region as a porous medium and treated the permeability to be either constant or varying in the radial direction. They solved the integral form of the momentum equation along with the Casson constitutive equation (the non-linear relation between shear stress and shear strain). This equation is given by:

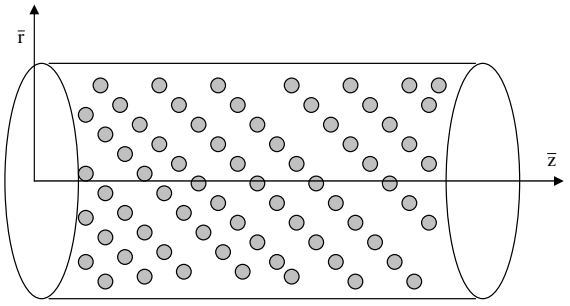

Fig. 5. Schematic diagram for blood flow clogged by fatty plaques and clots.

$$\bar{\tau}^{1/2} = \tau_y^{1/2} + \left[-\mu_\infty \frac{d\bar{u}}{d\bar{r}} \right]^{1/2}, \quad \text{if } \bar{\tau} \geqslant \tau_y$$
$$\frac{d\bar{u}}{d\bar{r}} = 0, \quad \text{if } \bar{\tau} \leqslant \tau_y \tag{12}$$

where τ_y and μ_∞ denote the fluid yield stress and Casson's viscosity (viscosity at high shear rate), respectively. The parameters $\bar{\tau}$, $\bar{u}$ and $\bar{r}$ denote the fluid shear stress, dimensional axial velocity and the dimensional radial coordinate, respectively. They obtained analytical solutions for the velocity distribution and found that the flow rate frictional resistance increases drastically with an increase in the yield stress and a decrease in the permeability.

Tada and Tarbell [33] utilized the Brinkman model to investigate the two-dimensional interstitial flow through the tunica media (fibrous outer layers of a bulb) of an artery wall in the presence of an internal elastic lamina (IEL). This lamina separates the tunica media from the subendothelial intima (inner layer of blood vessels). They modeled the IEL as an impermeable barrier to water flux except for fenestral pores which were uniformly distributed over the IEL. They treated the tunica media as a heterogeneous medium which contains a periodic array of smooth muscle cells (SMCs) implanted in a fibrous matrix. This can simulate the interstitial proteoglycan (higher molecular weight complex protein) and collagen fibers. They found that the average shear stress around the circumference of the SMC in the immediate vicinity of the fenestral pore could be 100 times greater than that around an SMC but away from the IEL in the fully developed interstitial flow region. These high shear stresses can affect SMCs physiological functions.

4.3. Generalized flow transport models in biological tissues

In cases where fluid inertia is not negligible, the form drag exerted by the fluid on the solid becomes significant. Vafai and Tien [34,35] arrived at a generalized model for flow transport in porous media which accounts for various pertinent effects. This generalized model is given by the following equation:

$$\frac{\rho_f}{\varepsilon}\left[\frac{\partial\langle \mathbf{V}\rangle}{\partial t} + \langle(\mathbf{V}\cdot\nabla)\mathbf{V}\rangle\right] = -\nabla\langle P\rangle^f + \frac{\mu}{\varepsilon}\nabla^2\langle\mathbf{V}\rangle - \frac{\mu}{K}\langle\mathbf{V}\rangle - \frac{\rho_f F\varepsilon}{K^{1/2}}[\langle\mathbf{V}\rangle\cdot\langle\mathbf{V}\rangle]\mathbf{J} \tag{13}$$

where F and ρ_f are the dimensionless inertia term coefficient and the fluid density, respectively. The parameters $\langle P\rangle^f$ and $\mathbf{J}$ are the average pressure inside the fluid and a unit vector oriented along the velocity vector $\mathbf{V}$, respectively. The quantities $\langle\mathbf{V}\rangle$, and $\langle(\mathbf{V}\cdot\nabla)\mathbf{V}\rangle$ are the local volume average of $\mathbf{V}$ and $(\mathbf{V}\cdot\nabla)\mathbf{V}$, respectively, associated with the fluid. This generalized model also accounts for the convective terms. This generalized model or a more limited form of it is also referred to as the Brinkman–Forchheimer–Darcy equation. There is a lack of biological studies that utilize the Brinkman–Forchheimer–Darcy model. It is important to utilize Eq. (13) in tissue media especially those located near the aortas or in skeletal tissues that have high perfusion rates. Table 2 summarizes the features of the different flow transport models described in this work. These features are discussed in details and summarized in works of Vafai and Tien [36] and Alazmi and Vafai [37,38].

5. Bioheat equation

Biological tissues contain dispersed cells separated by voids. Blood enter these tissues through vessels referred to as arteries and perfuse to the tissue cells via blood capillaries as shown in Fig. 6. Returned blood from the capillaries are accumulated in veins where the blood is pumped back to the heart. Energy transport in tissues is due to thermal conduction, blood perfusion and heat generation (e.g. metabolic heat generation). The energy transport in a biological system is usually expressed by the bioheat equation. The bioheat equation developed by Pennes [39] is one of the earliest models for energy transport in tissues (Fig. 6). Pennes considered all the properties appearing for the conduction and thermal storage terms to be for the tissue while he referred to the blood properties in the blood perfusion term. This term was modeled to be proportional to the difference between the arterial temperature and the temperature at a given location. Pennes assumed that the arterial blood temperature T_B is uniform throughout the tissue (Fig. 6) while he considered the vein temperature to be equal to the tissue temperature which is denoted by T at the same point. The equation that Pennes utilized is summarized as follows, in its simplest form:

$$\rho c_p \frac{\partial T}{\partial t} = k\frac{\partial^2 T}{\partial x^2} + c_{p_b} W_b (T_B - T) + q_m \tag{14}$$

Table 2
Summary of discussed and suggested flow transport models in porous media

Flow transport models	Equation	Features	Applications
Darcy model	Eq. (7)	• Simple • Considers Darcy resistance • Neglects boundary conditions • Neglects form drag • Neglects convective terms	Tumors, perfused muscle tissues, flow in soft connective tissues
Brinkman Model	Eq. (10)	• Considers Darcy resistance • Accounts for boundary conditions • Neglects form drag • Neglects convective terms	Vessels blocked by cholesterol and blood clots, muscles near artery
Brinkman–Forchheimer–Darcy Model (Generalized model)	Eq. (13)	• Considers Darcy resistance • Accounts for boundary conditions • Accounts for form drag • Accounts for convective terms	Suggested for high perfused skeletal tissues and biomedical applications encountering relatively large inertia effects

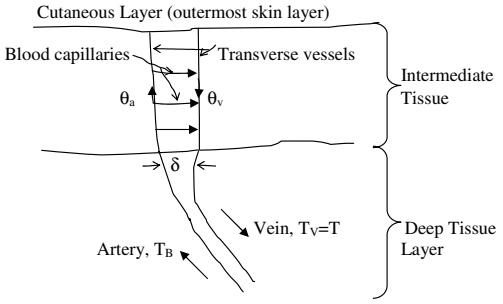

Fig. 6. Schematic diagram for the intermediate tissue of the skin.

where t, x, ρ, c_p, ρ_b, c_{p_b}, W_b, k and q_m are the time, space coordinate, tissue density, tissue specific heat, blood density, blood specific heat, blood volumetric perfusion rate, tissue thermal conductivity and heat generation within the tissue, respectively. Pennes equation has been utilized in various biological research works and is found to be quite useful because of its simplicity. An example of more recent research works utilizing Pennes equation is that of Zhu and Diao [40]. They used the Pennes equation to simulate the steady state temperature distribution within the brain after head injury. They determined where to place temperature sensors for infants and adults beneath the brain tissue in order to monitor the volumetric and average brain tissue temperature. Another example is the work of Deng and Liu [41]. They studied analytically using the Pennes equation the effect of pulsative blood perfusion on the tissue temperature.

Later Weinbaum and Jiji [42] utilized the hypothesis that small arteries and veins are parallel and the flow direction is countercurrent resulting in counterbalanced heating and cooling effects. This kind of tissue vascularization causes the isotropic blood perfusion term in the Pennes equation to be negligible and it causes the tissue to behave as an anisotropic heat transfer medium. Accordingly, Weinbaum and Jiji [42] modified the thermal conductivity in the Pennes equation by means of an "effective conductivity" related quadratically to blood perfusion rate which is affected by the dimensions and the directions of the vessels. They also showed that isotropic blood perfusion between the countercurrent vessels can have a significant influence on heat transfer in regions where the countercurrent vessels are under 70-μm diameter.

An important research work example that utilized Weinbaum and Jiji's [42] model is the work of Guiot et al. [43]. They used the Weinbaum and Jiji's model, assuming a linear relation between the effective thermal conductivity and the blood perfusion rate, to determine the increase in the thermal conductivity in a perfused tissue. Guiot et. al. reported an 11% increase in the thermal conductivity and their results suggested that in addition to a "temperature map", also "a perfusion map" within the heated volume should be monitored routinely throughout the hyperthermic sessions since the local value of perfusion can vary substantially within few centimeters. The importance of "effective thermal conductivity" was further revealed by Song et al. [44] who demonstrated that a tissue which exhibits only a small increase in the thermal conductivity due to countercurrent convection in its vasoconstricted state (narrowing of the blood vessel) can exhibit more than a fivefold increase in the thermal conductivity in its vasodilated state (during relaxation of the muscle).

Wissler [45] pointed that the Weinbaum and Jiji's [42] model assumes that the mean temperature in the neighborhood of an artery–vein pair is the arithmetic mean of the arterial and venous blood at the point of entry and that the temperature of blood draining into

veins from capillaries and small veins is equal to the temperature of venous blood at the point of entry, assuming there is very little heat transfer between thermally significant artery–vein pairs and the tissue. Wissler [45] indicated that these assumptions are questionable and the Weinbaum and Jiji's [42] model was derived for a subcutaneous region (tissues under the skin). Wissler [45] denoted that muscle and skin are rather different and a formulation appropriate for one may not be applicable for another biological tissue.

Baish [46] presented a new bioheat transfer model for a perfused tissue. He considered simulation of a realistic vascular tree containing all thermally significant vessels in a tissue using a physiologically-based algorithm. His model was based on solving the conjugate convection of the blood coupled to the three-dimensional conduction in the extravascular tissue while accounting for a statistical interpretation of the calculated temperature field. His work illustrates the dependence of the temperature distribution on the flow rate and the vascular geometry. He also illustrates that the Pennes formulation of the bioheat transfer equation accurately predicts the mean tissue temperature except when the arteries and veins are in closely spaced pairs. Baish's model is useful for fundamental studies of tissue heat transport. Baish suggested extending this work to other forms of tissue transport including oxygen, nutrient, and drug transport. For heat transfer in muscle tissues, Weinbaum et al. [47] found that a correction factor or efficiency needs to be multiplied by the perfusion source term in the Pennes equation for bioheat transfer in a muscle tissue. This coefficient is a function of the vascular cross-sectional geometry and is independent of the Peclet number. The value of this coefficient is found to vary between 0.6 and 0.7 for most muscle tissues.

5.1. Bioheat equation and transport through porous media

The real application of the porous media models and bioheat transfer in human tissues is relatively recent. Xuan and Roetzel [48,49] used the transport through porous media concepts to model the tissue–blood system composed mainly of solid particles (tissue cells) and interconnented voids that contain either arterial or venous blood. They utilized the principle of local thermal non-equilibrium between the tissue and the blood to formulate the thermal energy exchange between the tissue and the blood at a given location. This requires a system of two energy equations, one equation for the blood and the other for the peripheral skeletal tissue, to describe the energy exchange in the tissue.

5.1.1. Heat transfer equations for tissues

Xuan and Roetzel [48] utilized the local thermal non-equilibrium model as described in the works of Amiri and Vafai [50,51], Alazmi and Vafai [52] and Lee and Vafai [53] to model the heat transfer within the artery blood and the tissue. This model is summarized as follows:

$$\varepsilon(\rho c_{\mathrm{p}})_{\mathrm{b}}\left(\frac{\partial\langle T\rangle^{\mathrm{b}}}{\partial t}+\mathbf{u}_{\mathrm{b}}\cdot\nabla\langle T\rangle^{\mathrm{b}}\right)=\nabla\cdot\left(\mathbf{k}_{\mathrm{b}}^{\mathrm{a}}\cdot\nabla\langle T\rangle^{\mathrm{b}}\right)+h_{\mathrm{bs}}\left(\langle T\rangle^{\mathrm{s}}-\langle T\rangle^{\mathrm{b}}\right) \tag{15}$$

$$(1-\varepsilon)(\rho c_{\mathrm{p}})_{\mathrm{s}}\frac{\partial\langle T\rangle^{\mathrm{s}}}{\partial t}=\nabla\cdot\left(\mathbf{k}_{\mathrm{s}}^{\mathrm{a}}\cdot\nabla\langle T\rangle^{\mathrm{s}}\right)+h_{\mathrm{bs}}\left(\langle T\rangle^{\mathrm{b}}-\langle T\rangle^{\mathrm{s}}\right)+q_{\mathrm{m}}(1-\varepsilon) \tag{16}$$

where $\langle T\rangle^{\mathrm{b}}$, $\langle T\rangle^{\mathrm{s}}$, $\mathbf{k}_{\mathrm{b}}^{\mathrm{a}}$, $\mathbf{k}_{\mathrm{s}}^{\mathrm{a}}$, ε, $\mathbf{u}_{\mathrm{b}}$ and h_{bs} are the local arterial blood averaged temperature, local tissue averaged temperature, blood effective thermal conductivity tensor, tissue effective thermal conductivity tensor, porosity of the tissue, blood velocity vector and interstitial convective heat transfer coefficient, respectively. For isotropic conduction, $\mathbf{k}_{\mathrm{s}}^{\mathrm{a}}$ and $\mathbf{k}_{\mathrm{b}}^{\mathrm{a}}$ are related to the tissue porosity through the following relationships:

$$\mathbf{k}_{\mathrm{s}}^{\mathrm{a}}=(1-\varepsilon)k \tag{17}$$

$$\mathbf{k}_{\mathrm{b}}^{\mathrm{a}}=\varepsilon k_{\mathrm{b}} \tag{18}$$

where k and k_{b} are constants representing tissue and blood thermal conductivities, respectively. As seen from Eqs. (15) and (16), the energy equations for both phases are coupled by the interstitial convective heat transfer [50–52,54–56]. This term represents the heat transfer to the tissue due to blood convection. Xuan and Roetzel [48,49] considered an effective thermal conductivity for the blood in order to account for the blood dispersion. The concept of thermal dispersion is well established in the theory of porous media as presented in the works of Amiri and Vafai [50,51]. It is worth noting that Xuan and Roetzel [49] considered local thermal non-equilibrium between the artery blood, vein blood and the tissue in constructing their bioheat model which is based on the theory of porous media.

Xuan and Roetzel [48,49] indicated that much information is needed to solve the system of two phase energy equations such as thermal and anatomic properties of the tissue, interstitial convective heat transfer coefficients as well as the velocity field of the blood. Therefore, local thermal equilibrium may serve as a good approximation for the temperature field for certain applications involving blood vessels of small sizes as can be shown using Amiri and Vafai [50,51], Khanafer and Vafai [52] and Marafie and Vafai [53]. In these applications, the tissue and the blood temperatures are the same at any given location and Eqs. (15) and (16) reduce to the following equation:

$$\left[\rho c_{\mathrm{p}}(1-\varepsilon)+\rho_{\mathrm{b}}c_{\mathrm{p_b}}\varepsilon\right]\frac{\partial T}{\partial t}+\varepsilon(\rho c_{\mathrm{p}})_{\mathrm{b}}\mathbf{u}_{\mathrm{b}}\cdot\nabla T=\nabla([\mathbf{k}_{\mathrm{s}}^{\mathrm{a}}+\mathbf{k}_{\mathrm{b}}^{\mathrm{a}}]\cdot\nabla T)+q_{\mathrm{m}}(1-\varepsilon) \tag{19}$$

The second term on the left is responsible for heat transfer due to blood perfusion. The perfusion source term, H_p, in Pennes equation is equal to $H_P = \rho_b w_b c_{p_b}(T_B - T)$ where w_b is the flow rate of blood in the tissue per unit volume of tissue. This term was derived based on a uniform blood perfusion assumption.

In the absence of heat generation, the source term in Eq. (16) reduces to $H_S = h_{bs}/(1-\varepsilon)(\langle T\rangle^b - \langle T\rangle^s)$, when this equation is divided by $(1-\varepsilon)$, while it has the $H_E = -\varepsilon(\rho c_p)_b \mathbf{u}_b \cdot \nabla T$ form for Eq. (19). Pennes [39] indicated that the temperature of the venous blood leaving at a point is equal to the tissue temperature at that point under equilibrium conditions between the capillary tube and the tissue. He also considered the arterial temperature to be uniform throughout the tissue. As such, in our opinion, the local thermal equilibrium source term, H_E, reduces to $H_E = -[\rho_b (u_b)_{AVG} \varepsilon c_{p_b}/\delta](T - T_B)$ based on Pennes assumptions where δ and $(u_b)_{AVG}$ are the average spacing between the transverse blood vessels (artery and vein pairs, Fig. 6) and the average blood velocity within blood capillaries connecting the transverse blood vessels (Fig. 1), respectively. Since transverse blood vessels in the tissue (Fig. 1) are equally spaced [57], the volumetric blood perfusion in the Pennes equation is assumed to be constant and it is approximately equal to $W_p = \rho_b (u_b)_{AVG} \varepsilon c_{p_b}/\delta$ based on Eq. (19). The interstitial convective heat transfer source term, H_S, represents the actual blood perfusion term [48,49] for the Pennes bioheat equation. Under thermal equilibrium conditions, the heat transfer equation based on the theory of porous media is [37]

$$\left[\rho c_p (1-\varepsilon) + \rho_b c_{p_b} \varepsilon\right] \frac{\partial T}{\partial t} = \nabla([(1-\varepsilon)k + \varepsilon k_b]\nabla T) + \beta \frac{\rho_b (u_b)_{AVG} \varepsilon c_{p_b}}{\delta}(T_B - T) + q_m(1-\varepsilon) \quad (20)$$

The correction factor β is unity under Pennes assumptions while it is less than one in real application [47].

Eq. (20) utilizes effective values for the thermal capacitance as well as thermal conductivity for the tissue–blood medium. However, Pennes equation ignored the influence of blood thermal capacitance and thermal conductivity on the heat transfer. Moreover, the effective heat generation is reduced in Eq. (20) since metabolic heat generation occurs only in the tissue. Recently, Romer [58] indicated that thermal capacitance, thermal conductivity and the source term need to be averaged over the control volume. However, he did not include their relationship with respect to the blood vascular diameters and dimensions. In addition, the size of blood vessels within the tissue may be variable due to increases in vessel branches allowing for variable porosity. This causes the thermal capacitance to be anisotropic. It should be noted that the thermal conductivity of the blood usually contains a static component and a dispersive component as illustrated by Amiri and Vafai [50] and Eq. (20). This causes the tissue–blood medium to be anisotropic with respect to the thermal conductivity in addition to the corresponding anisotropy indicated by Weinbaum and Jiji [42] due to concurrent blood flows.

Recently, Shih et al. [59] tried to relate the theory of porous medium to heat transfer in tissues but he did not introduce the blood perfusion in the energy balance for the blood phase. That term is the interstitial convective heat transfer as in the work of Xuan and Roetzel [48,49]. It appears that the term $(1-\phi)W_b c_b(T - T_a)$ in Eq. (4) of the work of Shih et al. [59] need to be eliminated as seen in the work of Romer [58]. Although good agreement exists between results predicted from Pennes equation and experimental results [60,61], the assumption of uniform perfusion can lead to overestimated tissue temperatures. For example, Craciunescu et al. [62] in his work for optimizing thermal therapy showed that errors in temperature simulation can be reduced if a perfusion map replaces the uniform perfusion term. Even though the error can be reduced, still the difference between the experimental results and the simulations of bioheat equation can be relatively large for certain applications. Craciunescu et al. [62] illustrated that simulations of the combination between large traceable vessels and the perfusion map yield the best results when compared with MR thermometry for a patient with high-grade sarcoma (a form of cancer that arises in the supportive tissues such as bone, cartilage, fat or muscle). As such, developing advanced heat transfer models in tissues such as a porous medium model based on thermal non-equilibrium states between the blood and the tissue is an important task since it accounts for the blood convection inside the blood vessels embedded in the tissue. The summary of the previously discussed bioheat transfer models in this work are listed in Table 3. In Section 6, a concept related to flow instabilities caused by swimming of microorganisms is discussed. This concept is named bioconvection and is different from blood convection inside vessels.

6. Bioconvection

Bioconvection is a terminology assigned to pattern-forming motions which are set up as a result of hydrodynamic instabilities in suspensions of swimming microorganisms [63]. Examples of the patterns are shown for suspensions of motile algae and of bacteria. These suspensions swim upwards in all cases in still water while being slightly denser than the water. Pedley and Kessler [63] indicated that the upswimming causes cells to accumulate in a thin layer near the upper surface which becomes denser than lower regions. This density distribution is unstable, and convective motions are

Table 3
Summary of presented bioheat transfer models

Bioheat transfer model	Main features
Pennes [38]	• simple • based on uniform perfusion • it is not valid for all tissues
Weinbaum and Jiji [41]	• valid when arteries and veins are close leading to negligible blood perfusion effects • utilizes an effective conductivity as function of the perfusion rate
Wissler [44]	• avoids assumptions of the Weinbaum and Jiji's [41] model
Baish [45]	• complex and statistical based model • considers simulation of a realistic vascular tree containing all thermally significant vessels
Weinbaum et al. [46]	• includes an efficiency term in Pennes source term to make Pennes equation applicable to muscle tissues
Theory of porous media (Principle of local thermal equilibrium) Amiri and Vafai [50,51], Khanafer and Vafai [52], Marafie and Vafai [53], Alazmi and Vafai [37], Xuan and Roetzel [48,49]	• modifies Pennes equation by considering the following effects (a) variations in the tissue porosity (b) blood dispersion (c) considers effective tissue conductivity (d) considers effective tissue capacitance
Theory of porous media (Principle of local thermal non-equilibrium) Amiri and Vafai [50,51], Alazmi and Vafai [52], Khanafer and Vafai [54], Marafie and Vafai [55], Kuznetsov and Vafai [56], Xuan and Roetzel [48,49]	• exact blood perfusion is included • complex and require more flow and thermal information • considers (a) variations in the tissue porosity (b) blood dispersion (c) considers effective tissue conductivity (d) considers effective tissue capacitance

set up as in a shallow fluid heated from below. He pointed that there is another mechanism of instability, called gyrotaxis, which is unaffected by a horizontal surface and can operate in a deep fluid. This is a consequence of the fact that the cells at the bottom swim upwards in the first place. Their average swimming direction is determined by a balance between gravitational and viscous torques. The bacteria consume oxygen as they swim up. Therefore, the bioconvective motions carry oxygen around with them, thus changing the concentration gradient. Pedley and Kessler [63]. outlined the important features that a mathematical description of these flow instabilities must possess.

Kuznetsov and Jiang [64] formulated a new continuum model for bioconvection in a dilute suspension of swimming gravitactic microorganisms (microorganisms tend to swim against the gravity) in a porous medium. They investigated the existence and stability of a two-dimensional plume in a tall, narrow chamber with stress-free sidewalls. They utilized the Darcy model as well as a microorganism conservation equation. They found that there is a critical permeability below which there exist no bioconvection which causes the cells to accumulate in the top layer.

Later, Kuznetsov and Avramenko [65] obtained a criterion on stability of the bioconvection using linear stability analysis based on the Darcy model. This criterion gives the critical permeability of the porous medium through the cell eccentricity, average swimming velocity, fluid viscosity, and other relevant parameters. They found that when microorganisms are close to a spherical shape, the most unstable disturbances have a zero vertical wave number. However, if they are sufficiently elongated, the most unstable disturbances have a non-zero vertical number. Finally, mass transfer and flow induced by solutal buoyancy forces in biological tissues and their application to Magnetic Resonance Imaging (MRI) are acquiring increased attention in recent developments [66,67].

7. Concluding remarks

Significant applications of biomedical systems such as biological tissues include flow, heat and mass transfer through porous media. The transport theory in porous media involving various models such as Darcy and Brinkman models for momentum transport and local

thermal equilibrium for energy transport were found to be quite useful in describing different biological applications. These models were successfully utilized in analyzing biological tissues and systems and important findings were obtained. It was found that models for convective transport through porous media are widely applicable in the production of the osteoinductive material, simulation of blood flow of tumors and muscles and in modeling blood flow when fatty plaques of cholesterol and artery-clogging clots are formed in the lumen. On the other hand, the diffusive transport models were found to be mainly applicable in tissue regeneration and transport of drugs and nutrients to brain cells. Large number of applications are associated with heat transfer in tissues such as thermal simulations within the brain, hyperthermic sessions, heat transfer in muscle and skin tissues and thermal therapy applications. The necessity of using more advanced transport models such as the generalized flow model and the local non-thermal equilibrium heat transfer model in analyzing biological tissues was established.

References

[1] H.R.P.G. Darcy, Les Fontaines Publiques de la volle de Dijon, Vector Dalmont, Paris, 1856.

[2] D.D. Joseph, D.A. Nield, G. Papanicolaou, Nonlinear equation governing flow in a saturated porous medium, Water Resour. Res. 18 (1982) 1049–1052.

[3] H.C. Brinkman, A calculation of the viscous force exerted by a flowing fluid on a dense swarm of particles, Appl. Sci. Res. A 1 (1947) 81–86.

[4] M.D. Sherar, A.S. Gladman, S.R.H. Davidson, J. Trachtenberg, M.R. Gertner, Helical antenna arrays for interstitial microwave thermal therapy for prostate cancer: tissue phantom testing and simulations for treatment, Phys. Med. Biol. 46 (2001) 1905–1918.

[5] D.C. Sanyal, N.K. Maji, Thermoregulation through skin under variable atmospheric and physiological conditions, J. Theor. Biol. 208 (2001) 451–456.

[6] G.J. Galban, B.R. Locke, Analysis of cell growth in a polymer scaffold using a moving boundary approach, Biotechnol. Bioeng. 56 (1997) 422–432.

[7] G.J. Galban, B.R. Locke, Analysis of cell growth kinetics and substrate diffusion in a polymer scaffold, Biotechnol. Bioeng. 62 (1999) 121–132.

[8] K. Vafai, S. Whitaker, Simultaneous heat and mass transfer accompanied by phase change in porous insulations, ASME J. Heat Transfer 108 (1986) 132–140.

[9] C. Nicholson, Diffusion and related transport mechanism in brain tissue, Rep. Prog. Phys. 64 (2001) 815–884.

[10] A.W. El-Kerah, S.L. Braunstein, T.W. Secomb, Effect of cell arrangement and interstitial volume fraction on the diffusivity on monoclonal antibodies in tissue, Biophys. J. 64 (1993) 1638–1646.

[11] D.A. Lubarsky, L.R. Smith, R.N. Sladen, J.R. Mault, R.L. Reed, Defining the relationship of oxygen delivery and consumption—use of biologic system models, Journal of Surgical Research 58 (1995) 508–803.

[12] K. Whang, T.K. Goldstick, K.E. Healy, A biodegradable polymer scaffold for delivery of osteotropic factors, Biomaterials 21 (2000) 2545–2551.

[13] C. Nicholson, M.E. Rice, The migration of substances in the neuronal microenvironment, Ann. NY Acad. Sci. 181 (1986) 55–71.

[14] S. Woerly, P. Petrov, E. Sykova, T. Roitbak, Z. Simonova, A.R. Harvey, Neural tissue formation within porous hydrogels implanted in brain and spinal cord lesions: ultrastructural, immunohistochemical, and diffusion studies, Tissue Eng. 5 (1999) 467–488.

[15] W.S. Koegler, C. Patrick, M.J. Cima, L.G. Griffith, Carbon dioxide extraction of residual chloroform from biodegradable polymers, J. Biomed. Mater. Res. 63 (2002) 567–576.

[16] J.C. Gore, A.W. Anderson, M.D. Does, D.F. Gochberg, J.M. Joers, R.P. Kennan, E.C. Parsons, M. Schachter, The relationship of problems in biomedical MRI to the study of porous media, Magn. Reson. Imaging 19 (2001) 295–300.

[17] A.S. Goldestein, T.M. Juarez, C.D. Helmke, M.C. Gustin, A.G. Mikoa, Effect of convection on osteoblastic cell growth and function in biodegradable polymer foam scaffolds, Biomaterials 22 (2001) 1279–1288.

[18] A. Leitao, M. Li, A. Rodrigues, The role of intraparticle convection in protein adsorption by liquid chromatography using POROUS 20 HQ/M particles, Biochem. Eng. J. 11 (2002) 33–48.

[19] W.S. Kim, J.M. Tarbell, Prediction of macromolecular transport through the deformable porous media of an artery wall by pore theory, Kor. J. Chem. Eng. 13 (1996) 457–465.

[20] M. Klanchar, J.M. Tarbell, Modeling water-flow through arterial tissue, Bull. Math. Biol. 49 (1987) 651–669.

[21] J.M. Huyghe, D.H. Vancampen, Finite deformation-theory of hierarchically arranged porous solids. 2. Constitutive behavior, Int. J. Eng. Sci. 33 (1995) 1873–1886.

[22] W.J. Vankan, J.M. Huyghe, J.D. Janssen, A. Huson, W.J.G. Hacking, W. Schreiner, Finite element analysis of blood flow through biological tissue, Int. J. Eng. Sci. 35 (1997) 375–385.

[23] W.J. Vankan, J.M. Huyghe, M.R. Drost, J.D. Janssen, A. Huson, A finite element mixture model for hierarchical porous media, Int. J. Numer. Meth. Eng. 40 (1997) 193–210.

[24] S.L. Bulter, S.S. Kohles, R.J. Thielke, C. Chen, R. Vanderby, Interstitial fluid flow in tendons or ligaments: a porous medium finite element simulation, Med. Biol. Eng. Comput. 35 (1997) 742–746.

[25] J.W. Baish, P.A. Netti, R.K. Jain, Transmural coupling of fluid flow in microcirculatory network and interstitium in tumors, Microvasc. Res. 53 (1997) 128–141.

[26] X.X. Lei, W.Y. Wu, G.B. Wen, J.G. Chen, Mass transport in solid tumors (I)—fluid dynamics, Appl. Math. Mech.—Eng. Ed. 19 (1998) 1025–1032.

[27] M.F. Milosevic, A.W. Fyles, R.P. Hill, The relationship between elevated interstitial fluid pressure and blood flow in tumors: a bioengineering analysis, Int. J. Radiat. Oncol. Biol. Phys. 43 (1999) 1111–1123.

[28] L. Preziosi, A. Farina, On Darcy's law for growing porous media, Int. J. Non-linear Mech. 37 (2002) 485–491.

[29] H.C. Brinkman, On the permeability of media consisting of closely packed porous particles, Appl. Sci. Res. A 1 (1947) 81–86.
[30] J. Bear, Y. Bachmat, Introduction to Modeling of Transport Phenomena in Porous Media, Kluwer Academic, Dordrecht, 1990.
[31] S. Liu, J.H. Masliyah, Non-linear flows in porous media, J. Non-Newton. Fluid Mech. 86 (1999) 229–252.
[32] R.K. Dash, K.N. Mehta, G. Jayaraman, Casson fluid flow in a pipe filled with a homogeneous porous medium, Int. J. Eng. Sci. 34 (1996) 1145–1156.
[33] S. Tada, J.M. Tarbell, Interstitial flow through the internal elastic lamina affects shear stress on arterial smooth muscle cells, Am. J. Physiol.—Heart Circulat. Physiol. 278 (2000) H1589–H1597.
[34] K. Vafai, C.L. Tien, Boundary and inertia effects on flow and heat transfer in porous media, Int. J. Heat Mass Transfer 24 (1981) 195–203.
[35] K. Vafai, Convective flow and heat transfer in variable porosity media, J. Fluid Mech. 147 (1984) 233–259.
[36] K. Vafai, C.L. Tien, Boundary and inertia effects on convective mass transfer in porous media, Int. J. Heat Mass Transfer 25 (1982) 1183–1190.
[37] B. Alazmi, K. Vafai, Analysis of variants within the porous media transport models, J. Heat Transfer—Trans. ASME 122 (2000) 303–326.
[38] B. Alazmi, K. Vafai, Analysis of fluid flow and heat transfer interfacial conditions between a porous medium and a fluid layer, Int. J. Heat Mass Transfer 44 (2001) 1735–1749.
[39] H.H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physiol. 1 (1948) 93–122.
[40] L. Zhu, C. Diao, Theoretical simulation of temperature distribution in the brain during mild hypothermia treatment for brain injury, Med. Biol. Eng. Comput. 39 (2001) 681–687.
[41] Z.S. Deng, J. Liu, Blood perfusion-based model for characterizing the temperature fluctuation in living tissues, Physica 300 (2001) 521–530.
[42] S. Weinbaum, L.M. Jiji, A new simplified bioheat equation for the effect of blood flow on local average tissue temperature, J. Biomech. Eng.—Trans. ASME 107 (1985) 131–139.
[43] C. Guiot, E. Madon, D. Allegro, P.G. Pianta, B. Baiotto, P. Gabriele, Perfusion and thermal field during hyperthermia. Experimental measurements and modelling in recurrent breast cancer, Phys. Med. Biol. 43 (1998) 2831–2843.
[44] J. Song, L.X. Xu, D.E. Lemons, S. Weinbaum, Enhancements in the effective thermal conductivity in rat spinotrapezius due to vasoregulations, J. Biomech. Eng.—Trans. ASME 119 (1997) 461–468.
[45] E.H. Wissler, Comments on the new bioheat equation proposed by Weinbaum and Jiji, J. Biomech. Eng.—Trans. ASME 109 (1987) 226–232.
[46] J.W. Baish, Formulation of a statistical-model of heat-transfer in perfused tissue, J. Biomech. Eng.—Trans. ASME 116 (1994) 521–527.
[47] S. Weinbaum, L.X. Xu, L. Zhu, A. Ekpene, A new fundamental bioheat equation for muscle tissue. 1. Blood perfusion term, J. Biomech. Eng.—Trans. ASME 119 (1997) 278–288.
[48] Y.M. Xuan, W. Roetzel, Bioheat equation of the human thermal system, Chem. Eng. Technol. 20 (1997) 268–276.
[49] Y.M. Xuan, W. Roetzel, Transfer response of the human limb to an external stimulus, Int. J. Heat Mass Transfer 41 (1998) 229–239.
[50] A. Amiri, K. Vafai, Analysis of dispersion effects and nonthermal equilibrium, non-Darcian, variable porosity incompressible-flow through porous-media, Int. J. Heat Mass Transfer 37 (1994) 939–954.
[51] A. Amiri, K. Vafai, Transient analysis of incompressible flow through a packed bed, Int. J. Heat Mass Transfer 41 (1998) 4259–4279.
[52] B. Alazmi, K. Vafai, Constant wall heat flux boundary conditions in porous media under local thermal non-equilibrium conditions, Int. J. Heat Mass Transfer 45 (2002) 3071–3087.
[53] D.Y. Lee, K. Vafai, Analytical characterization and conceptual assessment of solid and fluid temperature differentials in porous media, Int. J. Mass Transfer 42 (1999) 423–435.
[54] K. Khanafer, K. Vafai, Isothermal surface production and regulation for high heat flux applications utilizing porous inserts, Int. J. Heat Mass Transfer 44 (2001) 2933–2947.
[55] A. Marafie, K. Vafai, Analysis of non-Darcian effects on temperature differentials in porous media, Int. J. Heat Mass Transfer 44 (2001) 4401–4411.
[56] A.V. Kuznetsov, K. Vafai, Analytical comparison and criteria for heat and mass transfer models in metal hydride packed beds, Int. J. Heat Mass Transfer 38 (1995) 2873–2884.
[57] L.M. Jiji, S. Weinbaum, D.E. Lemons, Theory and experiment for the effect of vascular microstructure on surface tissue heat transfer—Part II: Model formulation and solution, J. Biomech. Eng.—Trans. ASME 106 (1984) 331–341.
[58] R.B. Roemer, Engineering aspects of hyperthermia therapy, Ann. Rev. Biomed. Eng. 1 (1999) 347–376.
[59] T.C. Shih, H.S. Kou, W.L. Lin, Effect of effective tissue conductivity on thermal dose distributions of living tissue with directional blood flow during thermal therapy, Int. Commun. Heat Mass Transfer 29 (2002) 115–126.
[60] K.M. Sekins, J.F. Lehmann, P. Esselmann, D. Dundore, A.F. Emery, B.J. Delateur, W.P. Nelp, Local muscle blood-flow and temperature responses to 915 MHz diathermy as simultaneously measured and numerically predicted, Arch. Phys. Med. Rehab. 65 (1984) 1–7.
[61] R.B. Roemer, K. Forsyth, J.R. Oleson, S.T. Clegg, D.A. Sim, The effect of hydralazine dose on blood perfusion changes during hyperthermia, Int. J. Hyperther. 4 (1988) 401–415.
[62] O.I. Craciunescu, B.W. Raaymakers, A.N.T.J. Kotte, S.K. Das, T.V. Samulski, J.J.W. Lagendijk, Discretizing large traceable vessels and using DE-MRI perfusion maps yields numerical temperature contours that match the MR noninvasive measurements, Med. Phys. 28 (2001) 2289–2296.
[63] T.J. Pedley, J.O. Kessler, Bioconvection, Sci. Prog. 76 (1992) 105–123.

[64] A.V. Kuznetsov, N. Jiang, Numerical investigation of bioconvection of gravitactic microorganisms in an isotropic porous medium, Int. Commun. Heat Mass Transfer 28 (2001) 877–886.

[65] A.V. Kuznetsov, A.A. Avramenko, A 2D analysis of stability of bioconvection in a fluid saturated porous medium—estimation of the critical permeability value, Int. Commun. Heat Mass Transfer 29 (2002) 175–184.

[66] K. Khanafer, K. Vafai, A. Kangarlu, Water diffusion in biomedical systems as related to magnetic resonance imaging, Magnetic Resonance Imaging Journal 21 (2003) 175–184.

[67] K. Khanafer, K. Vafai, A. Kangarlu, Computational modeling of cerebral diffusion-application to stroke imaging, Magnetic Resonance Imaging Journal, in press.