DEVELOPMENT OF TRANSPORT PHENOMENA MATHEMATICAL MODELS FOR LINEAR AND CONCENTRIC MICRODIALYSIS PROBES WITH DIFFUSION-LIMITED AND CONVECTION-ENHANCED OPERATIONAL FEATURES

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LIST OF ABBREVIATIONS

APAP	acetaminophen
BMF	Bungay's Microdialysis Framework
CE	convection-enhanced
CFD	computational fluid dynamics
DL	diffusion-limited
ECS	extracellular space
EF	extraction fraction
FEM	finite element method
GUI	graphical user interface
HPLC	high-performance liquid chromatography
MWCO	molecular weight cut-off
NS	Navier-Stokes equations
OFM	open flow microperfusion
OM	optical microscope
PAN	polyacrylonitrile
PC	polycarbonate
PDE	partial differential equation
Pe	Péclet number
PES	polyethersulfone
PSA	probe surrounding area
Re	Reynolds number
RR	relative recovery
SEM	scanning electron microscopy

LIST OF SYMBOLS

A	surface area of semipermeable membrane (m^2)
c	molar concentration (mol m^{-3})
c_0	initial analyte concentration (mol m^{-3})
$c_{dialysate}$	analyte concentration in dialysate (mol m^{-3})
$c_{perfusate}$	analyte concentration in perfusate (mol m^{-3})
c_{PSA}	initial analyte concentration in PSA (mol m^{-3})
c_{site}	analyte concentration at target site (mol m^{-3})
C_f	empirical inertia coefficient
D	diffusivity of solute ($m^2\ s^{-1}$)
D_{AB}	diffusivity of chemical substance A in solvent B ($m^2\ s^{-1}$)
D_g	diffusivity of glucose ($m^2\ s^{-1}$)
D_m	diffusion coefficient of membrane ($m^2\ s^{-1}$)
D_{PL}	diffusivity of analytes in the probe lumen ($m^2\ s^{-1}$)
D_{PSA}	diffusivity of analytes in the PSA ($m^2\ s^{-1}$)
D_T	diffusion coefficient of tissue ($m^2\ s^{-1}$)
g	gravity constant (m s^{-2})
I	identity matrix
k	permeability (m^2)
k_B	Boltzmann constant (m^2 kg s^{-2} K^{-1})
K_0	mass transfer coefficient
L_c	characteristic length (m)
N_c	convective flux with respect to a stationary axis (mol $m^{-2}\ s^{-1}$)
N_d	diffusive flux with respect to a stationary axis (mol $m^{-2}\ s^{-1}$)
N_p	total flux in the probe lumen (mol $m^{-2}\ s^{-1}$)
p	pressure (kg $m^{-1}\ s^{-2}$)

Q	volumetric flow rate ($m^3\ s^{-1}$)
Q_0	initial perfused solution flow rate ($m^3\ s^{-1}$)
R	internal radius of connecting tube /inner shaft (m)
r	radial distance from centreline/axial-symmetrical interface (m)
r_p	average radius of membrane pore (m)
r_s	average radius of analyte molecules (m)
s	mass source of concerned substance ($kg\ m^{-3}\ s^{-1}$)
T	temperature (K)
u_0	average fluid velocity ($m\ s^{-1}$)
u_r	radial fluid velocity ($m\ s^{-1}$)
u_z	axial fluid velocity ($m\ s^{-1}$)
$\vec{u}$	fluid velocity vector ($m\ s^{-1}$)
$\vec{u}_L$	fluid velocity vector for linear probe model ($m\ s^{-1}$)
$\vec{u}_C$	fluid velocity vector for concentric probe model ($m\ s^{-1}$)
v	initial fluid velocity at inlet ($m\ s^{-1}$)
$V_{bp,B}$	molar volume of solvent B at its boiling point ($m^3\ mol^{-1}$)
ε	porosity
μ	dynamic viscosity of fluid ($kg\ m^{-1}\ s^{-1}$)
$\xi_{d,i}$	hindrance factor
ρ	fluid density ($kg\ m^{-3}$)
τ	membrane tortuosity
φ	ratio of extracellular space volume to in vivo target site volume
ψ	associate parameter of solvent interactions

PEMBANGUNAN MODEL MATEMATIK FENOMENA PENGANGKUTAN JISIM UNTUK KUAR MIKRODIALISIS LELURUS DAN SEPUSAT DENGAN MENGGUNAKAN CIRI KENDALIAN YANG TERHAD KEPADA RESAPAN DAN YANG DIPERTINGKATKAN DENGAN PEROLAKAN

ABSTRAK

Mikrodialisis merupakan satu teknik pensampelan yang terkenal dalam bidang penyelidikan perubatan, lazimnya digunakan untuk mengukur kepekatan bahan kimia dalam tisu. Namun, kelemahan utama teknik ini ialah jumlah bahan kimia yang dikumpulkan (iaitu perolehan) tidak konsisten. Ini turut menimbulkan komplikasi lain, seperti keperluan untuk mengendalikan pra-larian dan kalibrasi. Salah satu cara untuk menyelesaikan kelemahan ini adalah dengan memahami kebatasan pengangkutan jisim dalam sistem mikrodialisis dengan meneliti bagaimana setiap parameter operasi mempengaruhi perolehan mikrodialisis. Satu pendekatan umum adalah melalui pemodelan matematik. Walaupun sudah ada beberapa model matematik untuk mikrodialisis, model-model itu hanya menumpu untuk memberi nilai perolehan yang tepat, sementara ciri-ciri lain seperti aliran bendalir dalam mikrodialisis diabaikan. Objektif utama kerja penyelidikan ini adalah untuk membangunkan model-model matematik unsur terhingga yang dapat memberi simulasi yang tepat bagi susuk kepekatan dan aliran bendalir dalam mikrodialisis. Model-model ini dibina berdasarkan kuar mikrodialisis lelurus dan sepusat. Domain model-model ini tertumpu pada komponen utama mikrodialisis, iaitu kuar mikrodialisis, membran yang dipasang pada kuar, dan kawasan di sekitar kuar (PSA). PSA ini terdiri daripada medium tetap yang mengandungi analit untuk penyelidikan, iaitu glukosa. Pengangkutan jisim dalam model-model ini diwakili oleh persamaan perolakan dan resapan, manakala sifat aliran bendalir diwakili oleh persamaan Navier-Stokes. Hasil simulasi model-model yang dibentangkan

turut menunjukkan persetujuan yang baik dengan keputusan eksperimen. Analisis regresi antara perolehan simulasi dan perolehan eksperimen memberi nilai R-kuadrat ≥ 98.5% untuk setiap model. Dengan menggunakan model-model yang dibentangkan, kelebihan dan kelemahan setiap parameter operasi untuk persampelan mikrodialisis telah diteliti. Sebagai contohnya, pensampelan mikrodialisis untuk glukosa di bawah kadar aliran cecair perfusi 1.0 μL min^{-1} dengan menggunakan kuar mikrodialisis lelurus and sepusat (panjang membran 10 mm, pemotongan berat molekul 30 kDa) menghasilkan perolehan sebanyak 30.98% dan 36.67%. Mengurangkan kadar aliran cecair perfusi kepada 0.5 μL min^{-1} akan meningkatkan perolehan kepada 55.77% dan 60.72%, tetapi pada masa yang sama, masa pensampelan juga akan meningkat. Di samping itu, walaupun pengangkutan jisim melalui membran dalam kuar mikrodialisis secara tradisinya didefinisikan sebagai proses yang terhad kepada resapan, adalah ditunjukkan dalam kerja ini bahawa di bawah keadaan kadar aliran cecair perfusi dalam kuar yang tinggi, keliangan membran yang tinggi, dan saiz liang membran yang besar, perolakan akan akan menunjukkan pengaruh yang signifikasi kepada perolehan mikrodialisis. Dengan itu, persamaan resapan yang dipertingkatkan dengan perolakan adalah diperlukan untuk mewakili pengangkutan jisim merentasi membran dalam kuar mikrodialisis.

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ABSTRACT

Microdialysis is a well-known sampling technique in medical researches, most commonly used to measure the concentration of chemicals in the extracellular space of tissues. However, despite being a well-established technique, microdialysis often gives inconsistent amounts of chemicals collected from the sampling site (i.e. recovery). This would give rise to other complications, such as the requirement of pre-runs and calibrations. In order to resolve this issue, it is necessary to understand the mass transport limitations of microdialysis set-up, by scrutinizing how each operational and design parameters of the microdialysis set-up affect the recovery. One common approach is through mathematical modelling. Although there are already several mathematical modelling works on microdialysis, those works would focus only on providing accurate estimations of the recovery, while other features such as fluid flows are neglected. The main objective of this research work is to develop finite element mathematical models that could provide accurate simulations of concentration and fluid flow profiles for microdialysis. These models were constructed based on linear and concentric microdialysis probes. Modelling domain of these mathematical models would focus on the microdialysis probes, the membrane attached to the probes, and the probe surrounding area (PSA). The PSA for this research work is a quiescent medium filled with the analyte to be recovered, which is glucose. Mass transport properties in the models are represented by convection-diffusion equations, while fluid flows are represented by Navier-Stokes equations. It is shown that the developed mathematical