3D MODELING OF REACTION-DIFFUSION MECHANISM IN HETEROGENEOUS CELL ARCHITECTURE

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ABSTRACT: The manifold cell organization permitted extraneous hydrophobic compounds to react with the existing compounds inside the cell. The carcinogenic and lipophilic environmental toxins PAH provoked detrimental and noxious compounds in the interior of the cell. The cell sustained reaction and diffusion mechanism with those lipophilic compounds. The heterogeneous cell configuration grew into mosaic by virtue of the membranous architectures in the vicinity of the cytoplasm. The establishment of those conglomerate cytoplasmic membranous organelles in 2D axisymmetric geometry was absurd therefore 3D geometry was constructed. The model had been formulated in ComsolMultiphysics by adopting the homogenization approach. The counter collation of the simulated results of 3D and 2D axisymmetric model were investigated. The commendable affinity demonstrated by the results encouraged to extend the model by introducing diminutive cytoplasmic organelles in addition with more convoluted reaction chains.

Key words: Lipophilic, Reaction-diffusion mechanism, Polycyclicaromatic hydrocarbons, Heterogeneous.

INTRODUCTION

The primitive entity of the mosaic and minute composition of living organisms christened as cell are microscopic as they ranges few micrometers. Intracellular membranes establish the heterogeneous cell architecture. Despite the fact that the cell itself is few micrometers, it also accommodates numerous miniature and complicated architectures. The primary components of cell are: cellular membrane, cytoplasm, nuclear membrane and nucleus. The tiny organelles i.e. mitochondria, endoplasmic reticulum, golgi apparatus etc. inhabit the cytoplasm, embedded in aqueous region (Campbell*et al.*, 2006) attributes also membranous in architecture, in consequence of which the mathematical modeling of the heterogeneous cell eventually turns out complex, provided that the above mentioned complex cytoplasmic membranous structures i.e. the tiny organelles inside the cytoplasm are comprehended, the model will turn out more intricate.The conferred model is inquired by the reaction and diffusion of Polycyclic Aromatic Hydrocarbons in cell. 2D axisymmetric model was promoted by (Dreij *et al.*, 2011) comprehending reaction-diffusion mechanism. Taking into account the earlier model, the subsequent model is progressed to 3D inclusive of the entire processes incorporated by (Dreij *et al.*, 2011).

MATERIALS AND METHODS

In the model discussed in this paper, some basic assumptions were used, the details of which can be found in (Dreij *et al.,* 2011). Homogenization approach was emphasized for the cytoplasm in the interest to attenuate the intricacy of the model. Partial Differential Equations were formulated and were solved in the software named ComsolMultiphysics along with the geometry. Moreover, the results of the preceding (2D axisymmetric) and subsequent (3D) models were compared adjacently for the affirmation of the commenced 3D model.

The nature was encompassed by peculiar environmental toxins and lethal compounds among which PAHs were most familiar. These lipophilic attributed environmental toxins acknowledged the cell to react with DNA of the cell, where it formed DNA adduct. When coal, oil, fuel and natural gas encountered partial burning, it yielded PAHs which were carcinogenic (Moiz and George, 1995). In extra-cellular medium, cytoplasm and nucleus, PAH diolepoxide endured the hydrolysis process resulting in the production of PAH tetrol. Unaccompanied by the reaction, the membranes sustained alone the diffusion process, where themembranes were partitioned by partition coefficient. Thecytosol permittedPAH diol epoxide to react with glutathione conjugate (GSH) giving rise to diol epoxide conjugates (Dreij*et al.,* 2011). Involving the DNA inside nucleus, PAH diolepoxide counteredwith the DNA, forming DNA adduct which can alter the behavior of DNA and can be the cause of destruction of the cell (Thakker*et al.,*1985).

Quantitative Model

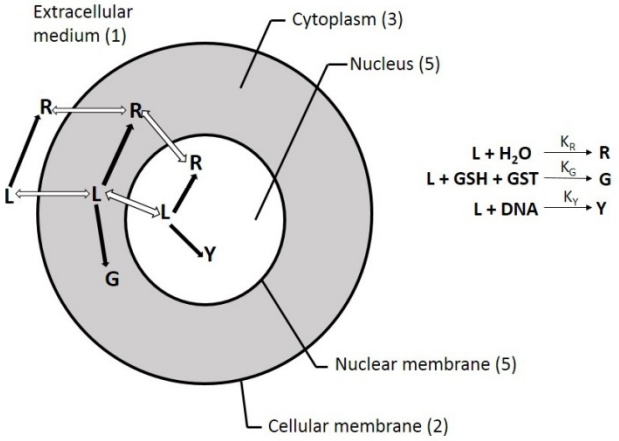

Figure-1 Showing the complete reaction and diffusion process within and outside the cell.

Table-1.Showing mathematical symbols/notations

Symbol	Description/ Chemical Name
L	PAH diol epoxide
R	PAH tetrol
G	Glutathione conjugate
Y	DNA adduct
⟹	Reaction
⟺	Diffusion

The Partial Differential Equations rising from Figure-1 are presented below:

Subdomain (Extra-cellular medium):

Subdomain 2 and 4 (Cellular and Nuclear membrane):

Subdomain 3 (Cytoplasm):

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The term " " used in the subscripts of the terms of above equations denoted the effective terms obtained by homogenization procedure, the details of which can be found in the study conducted by (Dreij *et al.,* 2011).

Subdomain (Nucleus):

Interface conditions: At the interface between aqueous and lipid part, we introduced the partition coefficient

Initial conditions: At initial time, we assumed that only was added to the system where its value in extra-cellular region was non-zero. The initial condition is presented below: at 0

The quantitative model along with the boundary and initial conditions as discussed abovewere formulated in Comsol Multiphysics 3.5 and Reaction Engineering Lab 1.5. This software worked on the principles of Finite Element Method (Chaskalovic, 2008). The model was generated in Chemical Engineering Module. The Direct Pardiso method was used for solving the problem.

RESULTS AND DISCUSSION

The mathematical model wasdesigned in Comsol Multiphysics 3.5 and Reaction Engineering Lab 1.5, the details of which were described in previous section. The geometric and chemical

Table-2. Geometric constants

Constants	Value
Volume of one cell[m^3]	$3x10^{-15}$
Volume of nucleus[m^3]	$7.5x10^{-16}$
Volume of cell medium[m^3]	10^{-5}
Thickness of membrane [m]	$1.127x10^{-8}$
Radius of cell [m]	$8.947x10^{-6}$

constantsderived here are in line with studies carried out by (Dreij *et al.,* 2011; Jernström *et al*., 1996;Sundberg *et al*., 2002) and are summarized in Table-2 and 3 respectively.

Table-3. Chemical Constants for the Model

Symbol	Constant	Value
D_1	Diffusion coefficient in extracellular medium [m^2s^{-1}]	10^{-9}
D_2,D_4	Diffusion coefficient in cell/nuclear membrane [m^2s^{-1}]	10^{-12}
D_5	Diffusion coefficient in nucleus [m^2s^{-1}]	$2.5x10^{-10}$
$K_{p,L}$	Partition coefficient for BPDE	$1.2x10^{-3}$
$K_{p,R}$	Partition coefficient for BPT	$8.3x10^{-3}$
k_R	Solvolytic reactivity forming Z [s^{-1}]	$7.7x10^{-3}$
k_Y	DNA adduct formation rate [s^{-1}]	$6.2x10^{-3}$
k_G	Formation rate of J	$3.7x10^3$

The numerical results were computed for a time span of 600sec. The results obtained from the 3D model discussed in this paper were compared with the numerical results of 2D axi-symmetric model which were found from (Dreij *et al.,* 2011). Figure-2 showed the comparison of degradation of PAH diol epoxides in extracellular medium of both models.Figure-3 represented the comparison of the formation of PAH tetrols, whereas in Figure-4, the comparison of PAH conjugated in nucleus was seen. Earlier, the study of computing the PAH diol epoxides in extracellular medium, PAH tetrols in extra and intra-cellular medium, and glutathione conjugate in cytoplasm was carried out by (Chaudhry *et al*., 2014) using the technique of differential transformation method, but in the current study the model developed was spatially distributed which resembled the in-vitro and in-vivo situation.

Figure-2: Showing comparison of PAH diol epoxide in extracellular medium

The bracketed letters p and n in the legends of the graphs represented the preceding 2D axi-symmetric model and subsequent 3D model respectively. L (p), R (p) and G (p) served as the results of 2D axi-symmetric in graph while L (n), R (n) and G (n) served as the graphs of 3D. The adjacent comparisons of graphs of both the models were coincidental.

Figure-3: Showing comparison of PAH tetrol in cell

The meager difference in the value of glutathione conjugate in graph in Figure-4 exhibitedmight be due to the modification in the dimension or the mesh establishment. These results represented the commendable affinity which stated that the model was valid for future consideration.

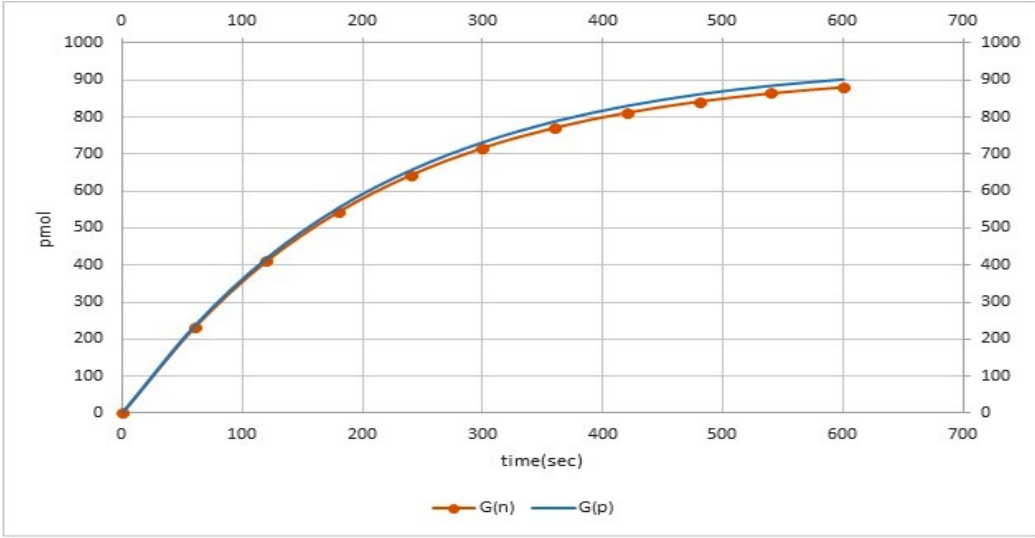

Figure-*4*: Showing comparison of Glutathione Conjugate in cytoplasm

Concerning the former model, we can extend it in either ways by recognizing these organelles as separate subdomains or inserting more reactions or membranes. To find the optimal parameter for the model using optimization approach is an important work to be done as discussed by (Dreij *et al.*, 2012; Chaudhry*et al*., 2009).

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