Agent Based Model of the Cytosine Radiation Induced Reaction

A L Rivera[1,2*], S Ramos-Beltran[1], A Paredes-Arriaga[1,3] and A Negron-Mendoza[1]

[1]*Institute of Nuclear Sciences. National Autonomous University of Mexico (UNAM), PO Box 70-543, 04510 Mexico City, Mexico*

[2]*Complexity Science Center, National Autonomous University of Mexico (UNAM)*

[3] *Sciences Faculty, National Autonomous University of Mexico (UNAM), 04510 Mexico City, Mexico*

*Email: ana.rivera@nucleares.unam.mx

ARTICLE INFORMATION

ABSTRACT

The stability of cytosine in aqueous solution was studied in the laboratory, simulating prebiotic conditions and using gamma radiation as an energy source, to describe cytosine behavior under radiation. For a better understanding of the radiation-induced processes, we proposed a mathematical model that considers chemical reactions as nonlinear ordinary differential equations. The radiolysis can be computationally simulated by an agent-based model, wherein each chemical species involved is considered to be an agent that can interact with other species with known reaction rates. The radiation is contemplated as a factor that promotes product formation/destruction, and the temperature determines the diffusion speed of the agents. With this model, we reproduce the changes in cytosine concentration obtained in the laboratory under different irradiation conditions.

1. Introduction

Radiation-induced oxidation reactions are a crucial process in understanding the formation of biologically relevant molecules in planets and icy bodies such as comets [1-4]. Primitive Earth and astrophysical conditions for these processes are difficult to simulate in the laboratory. There are few experimental setups studying the stability and formation of some compounds of biological importance under a high radiation field [5, 6]. In these experiments, changes induced by ionizing radiation can be quantified by dose measurements that indicate the amount of energy deposited on the samples by the gamma radiation. The first experiment of prebiotic synthesis was proposed by Miller [7], where several amino acids were synthesized from different gases in a primitive reducing atmosphere (H_2O, CH_4, NH_3, H_2) and electric discharges. Prebiotic importance for molecules specially RNA was established by Gilbert [8]. One component of RNA and DNA is cytosine, a pyrimidine base, but there are few experiments about the stability of cytosine ($C_4H_5N_3O$) under radiation, the molecule of interest in this work.

The irradiation of cytosine in aqueous solution involves the interaction of cytosine molecules with the different species formed by the radiation-induced decomposition of water (H, ·OH, e_{aq}^-, H_2, and H_2O_2). To describe the products generated by the interaction of the different species under radiation in an aqueous medium, we propose a mathematical model that describes the mass balance of all species involved, considering chemical reactions as nonlinear ordinary differential equations (NODE) [6, 9]. This model is complicated due to the significant number of reactions involved, the coupling between equations, and by the fact that all the NODEs need to be solved simultaneously. Moreover, the non-linear character of the equations makes the model strongly dependent on initial conditions. To circumvent these issues, some authors have used Monte-Carlo simulations [10]. We have proposed an agent-based model [11, 12] to simulate the chemical evolution of oxidation reactions of ferrous ions under radiation. The model is a modified version of the prey-predator model [13, 14] in which the mass-balance equation includes sink terms (all the reactions leading to destruction that can be considered prey) and source terms (all the reaction rates leading to production that can be interpreted as predators). In this model, each chemical species involved is considered as an agent that can interact with other species with known reaction rates, radiation is taken as a factor that promotes a product's formation/destruction, and the temperature determines the diffusion speed of the agents. Here, we modify the model to reproduce the radiation-induced reaction of cytosine in aqueous solution.
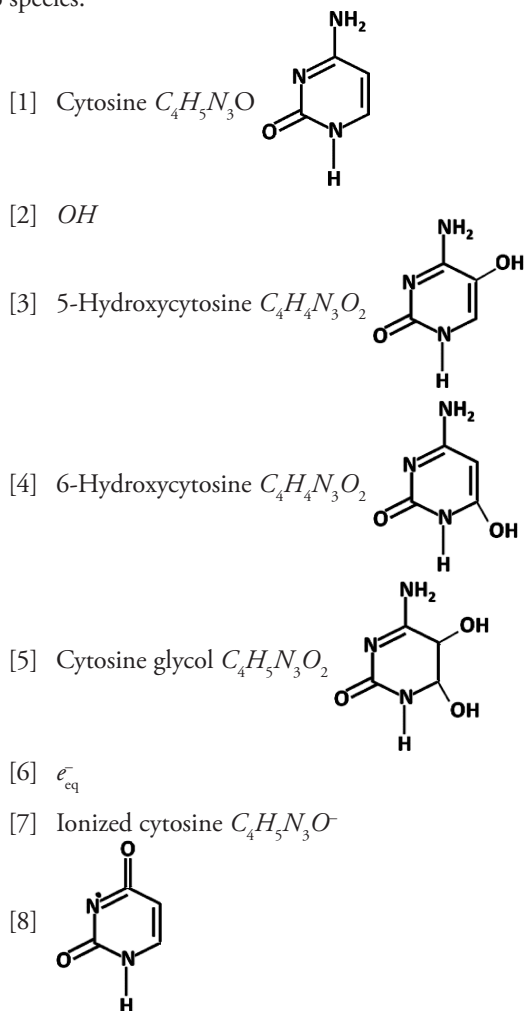
2. Experimental Setup

The experimental setup followed the setups of [14, 15]. Aqueous solutions of 5×10^{-4} M of cytosine were irradiated with a Cobalt 60 source at an irradiation dose ranging from 1 to 5 kGy. The samples were in Pyrex cells at room temperature (295 K), oxygen-free. After irradiation, the samples were analyzed by UV-Vis spectroscopy at 275 nm (the peak wavelength associated with cytosine [16]) in a Varian Cary100 spectrophotometer (California USA). Cytosine concentrations were determined and compared with a modified version of the agent-based model programmed with Python in [11, 12].
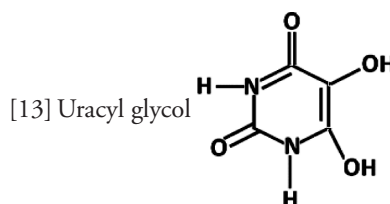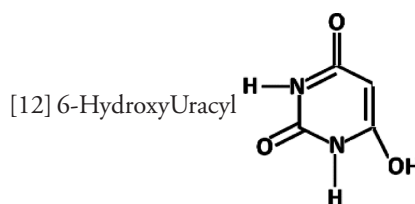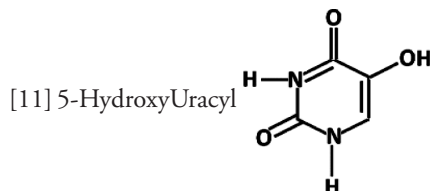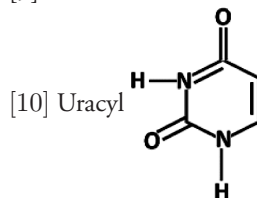
3. Model for Radiation Induced Reaction of Cytosine

3.1 Chemical Reaction Model

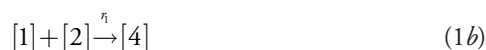Chemical reactions involved on cytosine production involve 16 species:

[1] Cytosine $C_4H_5N_3O$

[2] OH

[3] 5-Hydroxycytosine $C_4H_4N_3O_2$

[4] 6-Hydroxycytosine $C_4H_4N_3O_2$

[5] Cytosine glycol $C_4H_5N_3O_2$

[6] e_{eq}^-

[7] Ionized cytosine $C_4H_5N_3O^-$

[8]

[9] $H°$

[10] Uracyl

[11] 5-HydroxyUracyl

[12] 6-HydroxyUracyl

[13] Uracyl glycol

The chemical reactions involved in our cytosine experiment starts with a reaction that can occur with a probability of 87%:

$$[1]+[2]\xrightarrow{r_1}[3] \qquad (1a)$$

or a reaction that occurs with a probability of 10%:

$$[1]+[2]\xrightarrow{r_1}[4] \qquad (1b)$$

Then the following reactions occur:

$$[3]+[2]\xrightarrow{r_2}[5] \qquad (1c)$$

$$[4]+[2]\xrightarrow{r_2}[5] \qquad (1d)$$

$$[1]+[6]\xrightarrow{r_3}[7] \qquad (1e)$$

$$[8]+[9]\xrightarrow{r_5}[10] \qquad (1f)$$

Now the next reaction can occur with a probability of 82%:

$$[10]+[2]\xrightarrow{r_6}[11] \tag{1g}$$

or the reaction with a probability of 18%:

$$[10]+[2]\xrightarrow{r_6}[12] \tag{1h}$$

Afterwards the next reactions occur:

$$[11]+[2]\xrightarrow{r_7}[13] \tag{1i}$$

$$[12]+[2]\xrightarrow{r_7}[13] \tag{1j}$$

with the six known reaction rates:

$$r_1 = 6.3\times10^9, \tag{2a}$$

$$r_2 = 3.1\times10^9, \tag{2b}$$

$$r_3 = 13\times10^9, \tag{2c}$$

$$r_5 = 0.47\times10^9, \tag{2d}$$

$$r_6 = 5.7\times10^9, \tag{2e}$$

$$r_7 = 3.0\times10^9. \tag{2f}$$

3.2 Mathematical Model

Kinetics of the radiation induced chemical reactions in a thermal bath (Eqs. 1) involves the mass balance for each of the 13 species. This balance, assuming that is due with the interaction between pairs, can be described by coupled nonlinear differential equations considering external source (radiation and bath temperature), production (source terms) and destruction (sink terms), as proposed on a previous work [6]:

$$\frac{dN_i(t)}{dt} = f_i + \sum_j\sum_k r_{j,k}^{(i)}N_j(t)N_k(t) - N_i(t)\sum_m r_{i,m}^{(i)}N_m(t), \tag{3}$$

where N_i denotes the molar concentration of the i-species at time t, $r_{j,k}^{(i)}$ denotes the reaction rate constant for the two-reactive species j, k, that produce the specie (i), and f_i is an external source given by:

$$f_i(I_d, T) = \frac{6.2\times10^{11}}{3.6\ N_A}\frac{M_i}{M_{H_2O}}\ G_i e - \frac{M_i}{2\ N_A\ k\ T}I_d, \tag{4a}$$

where M_i is the molecular mass of the specie (i), M_{H_2O} is the molecular mass of water (18.02 g/mol), N_A is the Avogadro number 6.022×10^{23} mol, k is the Boltzmann constant 1.38×10^{-23} m²kgs⁻²K⁻¹, and G_i is the radiochemical constant that gives the number of species (i) produced when 100 eV are absorbed by the system. For the case of cytosine, G_i is 4.42 molecules, then:

$$f_i(I_d, T) = [7.01 - 2.04I_d]\times10^{-4}\ M_i, \tag{4b}$$

Chemical reactions described by the system of Eqs. (1) can be rewritten using Eqs. (3) and (4) as the following NODE system:

$$\frac{d[1]}{dt} = f_1 - r_1[1][2] - r_3[1][6], \tag{5a}$$

$$\frac{d[2]}{dt} = f_2 - r_1[1][2] - r_2[3][2] - r_2[4][2] - r_6[10][2] \\ - r_7[11][2] - r_7[12][2], \tag{5b}$$

$$\frac{d[3]}{dt} = f_3 + r_1[1][2] - r_2[3][2], \tag{5c}$$

$$\frac{d[4]}{dt} = f_4 + r_1[1][2] - r_2[4][2], \tag{5d}$$

$$\frac{d[5]}{dt} = f_5 + r_2[3][2] + r_2[4][2], \tag{5e}$$

$$\frac{d[6]}{dt} = f_6 - r_3[1][6] + r_2[4][2], \tag{5f}$$

$$\frac{d[7]}{dt} = f_7 + r_3[1][6], \tag{5g}$$

$$\frac{d[8]}{dt} = f_8 - r_5[8][9], \tag{5h}$$

$$\frac{d[9]}{dt} = f_9 - r_5[8][9], \tag{5i}$$

$$\frac{d[10]}{dt} = f_{10} + r_5[8][9] - r_6[10][2], \tag{5j}$$

$$\frac{d[11]}{dt} = f_{11} + r_6[10][2] - r_7[11][2], \tag{5k}$$

$$\frac{d[12]}{dt} = f_{12} + r_6[10][2] - r_7[12][2], \tag{5l}$$

$$\frac{d[13]}{dt} = f_{13} + r_7[11][2] + r_7[12][2], \tag{5m}$$
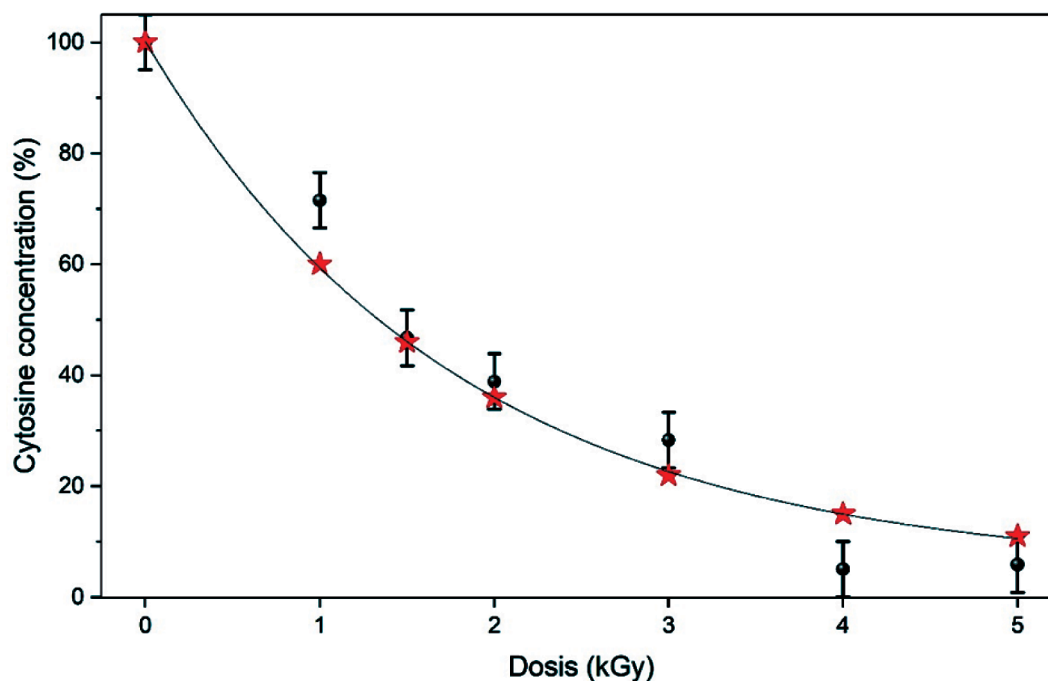
Figure 1. Cytosine concentration as function of the radiation doses.

3.3 Agent-Based Model

The coupled system of Eqs. (5) can be solved using an agent-based model like the prey-predator one that we developed in previous works [11, 12] where we generated a Python code to evaluate the molar concentrations of each species. In Fig. 1 is plotted the cytosine concentration obtained by the code comparing the values with the experimental ones for different radiation doses. As we see our numerical result closely resembles the experimental one, with a difference of less than 10%. Red stars are concentrations from the agent-based model and black dots from experimental data.

4. Conclusion

Cytosine reactions induced by gamma radiation at room temperature were studied and compared with the concentrations determined by an agent-based model. The model evaluates the concentration of products generated by the interaction of different reactive free-radicals under radiation. It involves the mass balance of 16 species, considering each species as an agent that can interact with other species with known reaction rates. Interactions lead to destruction (prey) and production (predator) terms, with radiation considered as a factor that affects product formation. This simple and robust model agrees with the experimental results. Both approaches showed that cytosine decomposed rapidly in a high radiation field environment, and that for the survival of this molecule and its further participation in the formation of more complex molecules, it is necessary to have a protection mechanism, such as the adsorption in clay minerals.

Acknowledgements

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