# Modeling of Processes Running in Radical Clusters Formed by Ionizing Radiation with the Help of Continuous Petri Nets and Oxygen Effect

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*Abstract*—The final biological effect of ionizing particles may be influenced strongly by some chemical substances present in cells mainly in the case of low-LET radiation. The influence of oxygen may by particularly important because oxygen is always present in living cells. The corresponding processes are then running mainly in the chemical stage of radiobiological mechanism.

The radical clusters formed by densely ionizing ends of primary or secondary charged particles are mainly responsible for final biological effect. The damage effect depends then on radical concentration at a time when the cluster meets a DNA molecule. It may be strongly influenced by oxygen present in a cell as oxygen may act in different directions: at small concentration of it the interaction with hydrogen radicals prevails while at higher concentrations additional efficient oxygen radicals may be formed.

The basic radical concentration in individual clusters diminishes, which is influenced by two parallel processes: chemical reactions and diffusion of corresponding clusters. The given simultaneous evolution may be modeled and analyzed well with the help of Continuous Petri nets. The influence of other substances present in cells during irradiation may be studied, too. Some results concerning the impact of oxygen content will be presented.

*Keywords*—DSB formation, chemical stage, Petri nets, radiobiological mechanism.

## I. INTRODUCTION

THE biological effect of ionizing particles consists in principle always of three stages; physical, chemical and biological. The damage of DNA molecules in individual cells under standard conditions is to be caused by different radicals formed in corresponding water medium, as direct effect caused by primary or secondary charged particles may be practically neglected. The biologically efficient damage of DNA molecules (formation of DSB mainly at lower-LET radiation) may be then given by radicals formed in clusters by densely ionizing track ends of individual particles. Before meeting a DNA molecule these radicals react mutually or with some other species being present in corresponding water medium; the number of efficient radicals may be lowered or heightened by these additional reactions.

In the following the cluster (at low-LET radiation) will be described (for simplicity) as spherically symmetric system.

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Two main parallel processes will be assumed to be running within a cluster: chemical reactions of radicals having been formed at energy transfer and contemporary cluster diffusion. The dynamics of chemical reactions depends then on cluster diffusion due to the concentration change of corresponding chemical species. Both the parallel processes will be then simulated with the help of Continuous Petri nets.

Continuous Petri nets consist of three main elements: places, transitions and arcs. The places represent the state of the system. Each place is marked by a real number, which determines the amount (value) of monitored parameter (e.g., the concentration of a chemical substance in a volume, etc.). The real number determining the state of a monitored place can be changed via transitions. The dynamic change of a place is given by corresponding transitions determined with the help of differential equations. Each place can be changed only via the transitions which are linked to it. The dynamic changes of all places caused by the corresponding transitions occur simultaneously. It is similar process as solving a system of differential equations with the difference that here we do not have anything complicated to program and debug.

## II. MATHEMATICAL MODEL OF PROCESSES RUNNING IN DIFFUSING CLUSTERS

To establish the influence of the cluster diffusion (on corresponding changes of concentrations) we shall assume for simplicity that this diffusion goes in a limited spherical volume [8]. The time dependence of the diffusion process may be then described with the help of partial differential equations

$$\frac{\partial c_i}{\partial t} = D_i \frac{1}{r^2} \frac{\partial}{\partial r}\left(r^2 \frac{\partial c_i}{\partial r}\right), \tag{1}$$

where $c_i(r,t)$ represent the time dependences of concentration distributions of individual species $i$, $r$ denoting the distance from the cluster center. By solving this equation one obtains

$$c_i(r,t) = \frac{N_i}{8\sqrt{(\pi D_i t)^3}} \exp\left(-\frac{r^2}{4D_i t}\right), \tag{2}$$

where $D_i$ are corresponding diffusion coefficients and $t$ is the time from the start of the diffusion in the theoretical center of the given cluster. The average cluster radius equals then

$$\bar{r}_i(t) = \frac{1}{N_i} \int_0^\infty r c_i(r,t) 4\pi r^2 dr, \tag{3}$$

or

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$$\bar{r}_i(t) = \frac{\pi}{2\sqrt{(\pi D t)^3}} \int_0^\infty r^3 \exp\left(-\frac{r^2}{4Dt}\right) dr, \qquad (4)$$

and the time dependence of the cluster volume may be then defined as

$$V_i(t) = \frac{4}{3}\pi \bar{r}_i^3(t), \qquad (5)$$

or

$$V_i(t) = \frac{256}{3}\sqrt{\left(\frac{D_i^3 t^3}{\pi}\right)}. \qquad (6)$$

Differentiating (6) we obtain

$$\frac{dV_i(t)}{dt} = 128\sqrt{\left(\frac{D_i^3 t}{\pi}\right)}. \qquad (7)$$

The given formulas ((6) and (7)) may be accepted as sufficient for characterizing the influence of diffusion process at least in the first approximation (even if the cluster diffusion will not go in fully spherically symmetrical way).

As the size of the cluster is small (about tens of nm), the concentration profile of radicals in clusters may be assumed to be Gaussian, and it is then possible to introduce average cluster concentrations $\bar{c}_i(t)$ of individual species:

$$\bar{c}_i(t) = \frac{N_i(t)}{V_i(t)}, \qquad (8)$$

where $N_i(t)$ is the number of corresponding chemical species in a cluster at a given instant and $V_i(t)$ describes the time dependence of cluster volume established according (6), which may be regarded as sufficient approximation for simulating the dynamics of chemical processes in diffusing clusters.

The average concentration change of individual chemical substances at any time may be then given as the sum of two independent processes (diffusion + chemical reactions).One can write

$$\frac{d\bar{c}_i(t)}{dt} = -\frac{c_i}{V_i}\frac{dV_i}{dt} - k_{ij}\bar{c}_i(t)\bar{c}_j(t), \qquad (9)$$

for the decrease of species $i$ due to reactions with any species $j$ and

$$\frac{d\bar{c}_i(t)}{dt} = -\frac{c_i}{V_i}\frac{dV_i}{dt} - k_{jk}^{(i)}\bar{c}_j(t)\bar{c}_k(t), \qquad (10)$$

for the increase of species $i$ due to mutual reactions between species $j$ and $k$. The first term of the right-hand side of (9) and (10) represent the diffusive contribution to the evolution of $c_i$. Using then (8) one obtains the system of partial differential equations

$$\frac{dN_i(t)}{dt} = -k_{ij}\frac{N_i(t)N_j(t)}{V_j(t)}, \qquad (11)$$

$$\frac{dN_i(t)}{dt} = V_i(t)k_{jk}^{(i)}\frac{N_j(t)N_k(t)}{V_j(t)V_k(t)}, \qquad (12)$$

that describes the dynamics of chemical reactions at any time $t$ when the influence of cluster diffusion is respected.

We will now simulate the dynamics of chemical processes with the help of continuous Petri nets. The time change of the continuous places $P_i$ is via continuous transitions $T_{i+j}$. According to (11) and (12) we can express the time change of the number of species $i(N_i)$ with the help of the set of continuous transitions $T_{j+k}$ in form

$$\frac{dN_i(t)}{dt} \equiv T_{(i+j)}^{(i)} = -k_{ij}\frac{N_i(t)N_j(t)}{V_j(t)}, \qquad (13)$$

or

$$\frac{dN_i(t)}{dt} \equiv T_{(j+k)}^{(i)} = V_i(t)k_{jk}^{(i)}\frac{N_j(t)N_k(t)}{V_j(t)V_k(t)}, \qquad (14)$$

The transition (13) expresses the speed of the number decrease of species $i(N_i)$ due to reaction of species $i$ with species $j$ and the transition (14) expresses the speed of the number increase of species $i(N_i)$ due to reaction of species $j$ with species $k$ for $j, k \neq i$.

It is, of course, necessary to use the value of volume $V_i$, which corresponds to individual species $i$ as the result of diffusion into the surrounding. The increase of this volume occurs via continuous transitions $T_i$ according to (7)

$$\frac{dV_i(t)}{dt} \equiv T_i = 128\sqrt{\left(\frac{D_i^3 t}{\pi}\right)}. \qquad (15)$$

We can express the continuous places and continuous transitions graphically (see Fig. 2).Places being represented by circles and transitions by rectangles. Circles with rectangles are joined by arcs.
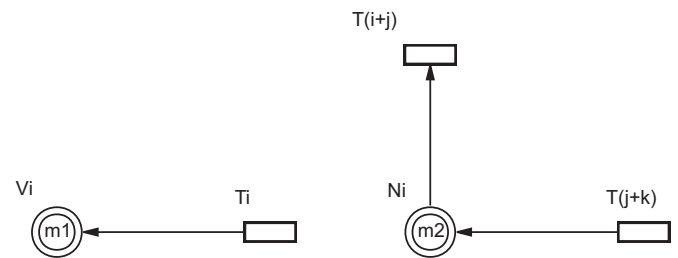


Fig. 1 Simple Petrinets

### III. Specification of the Model according to Data Kind

We shall assume that the radicals shown in Table I may be responsible for radiobiological effect; their diffusion coefficients taken from the literature having been introduced. As to the initial content of radicals in individual clusters we shall assume that the following species will be present: $H^\bullet$, $OH^\bullet$, $e_{aq}^-$ and $H_3O^+$. Considered chemical reactions are then introduced in Table II; the reaction rates (taken from the literature) are also given in this table [6].

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TABLE I
DIFFUSION COEFFICIENTS [7]

| Substance | Diffusion coefficient $(nm^2.ns^{-1})$ | Species amount | Designation of diff. coefficients |
|---|---|---|---|
| 1. $H^\bullet$ | 7.0 | $N_H$ | $D_H$ |
| 2. $OH^\bullet$ | 2.2 | $N_{OH}$ | $D_{OH}$ |
| 3. $e_{aq}^-$ | 4.9 | $N_e$ | $D_e$ |
| 4. $HO_2^\bullet$ | 2.3 | $N_O$ | $D_O$ |
| 5. $H_3O^+$ | 9.5 | $N_{H_3O}$ | $D_{H_3O}$ |
| 6. $O_2^-$ | 1.8 | $N_{O_2^-}$ | $D_{O_2^-}$ |
| 7. $OH^-$ | 5.3 | $N_{OH^-}$ | $D_{OH^-}$ |

The whole process dynamics is expressed graphically by continuous Petri nets in Fig. 2, where the places are marked as H, OH, e, O, H3O, O2M, OHM and O2 which represent individual species $H^\bullet$, $OH^\bullet$, $e_{aq}^-$, $HO_2^\bullet$, $H_3O^+$, $O_2^-$, $OH^-$ and $O_2$.

TABLE II
RECOMBINATION REACTION [6]

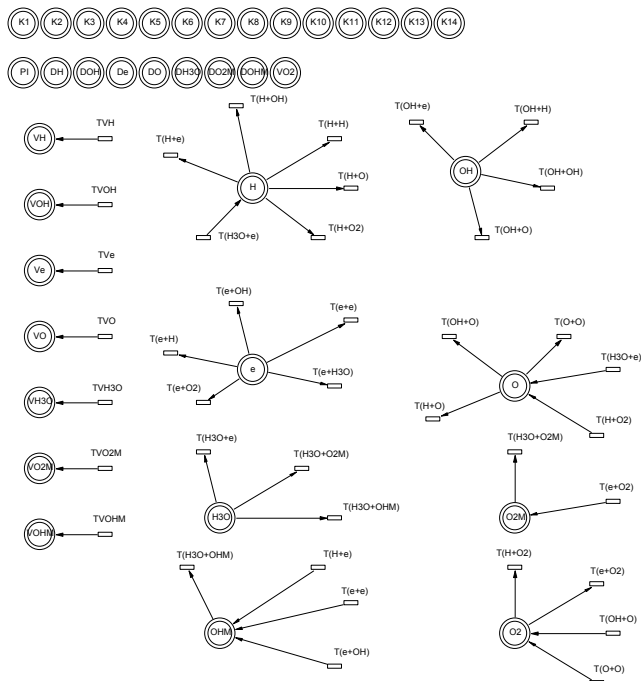| | Reaction | | Rate constants $(dm^3.mole^{-1}.s^{-1})$ |
|---|---|---|---|
| $k_1$ | $H^\bullet + H^\bullet \rightarrow$ | $H_2$ | $10 \times 10^{10}$ |
| $k_2$ | $e_{aq}^- + H^\bullet \rightarrow$ | $H_2 + OH^-$ | $2.5 \times 10^{10}$ |
| $k_3$ | $e_{aq}^- + e_{aq}^- \rightarrow$ | $H_2 + 2OH^-$ | $6 \times 10^9$ |
| $k_4$ | $e_{aq}^- + OH^\bullet \rightarrow$ | $OH^- + H_2O$ | $3 \times 10^{10}$ |
| $k_5$ | $H^\bullet + OH^\bullet \rightarrow$ | $H_2O$ | $2.4 \times 10^{10}$ |
| $k_6$ | $OH^\bullet + OH^\bullet \rightarrow$ | $H_2O_2$ | $4 \times 10^{10}$ |
| $k_7$ | $H_3O^+ + e_{aq}^- \rightarrow$ | $H^\bullet + H_2O$ | $2.3 \times 10^{10}$ |
| $k_8$ | $HO_2^\bullet + H^\bullet \rightarrow$ | $H_2O_2$ | $1 \times 10^{10}$ |
| $k_9$ | $e_{aq}^- + O_2 \rightarrow$ | $O_2^- + H_2O$ | $1.9 \times 10^{10}$ |
| $k_{10}$ | $HO_2^\bullet + OH^\bullet \rightarrow$ | $H_2O + O_2$ | $1 \times 10^{10}$ |
| $k_{11}$ | $HO_2^\bullet + HO_2^\bullet \rightarrow$ | $H_2O_2 + O_2$ | $2 \times 10^6$ |
| $k_{12}$ | $H^\bullet + O_2 \rightarrow$ | $HO_2^\bullet$ | $1 \times 10^{10}$ |
| $k_{13}$ | $O_2^- + H_3O^+ \rightarrow$ | $HO_2^\bullet$ | $3 \times 10^{10}$ |
| $k_{14}$ | $H_3O^+ + OH^- \rightarrow$ | $H_2O$ | $3 \times 10^{10}$ |



Fig. 2 Petrinets

The suggested mathematical approach enables us to describe time evolution of processes running in individual radical clusters during the chemical stage of water radiolysis. The final effect of this stage has been studied by us on the basis of corresponding differential equations already earlier [1]. Now we should like to show that with the help of Continuous Petri nets more detailed analysis may be performed.

The aim of this paper is to demonstrate mainly the possible contribution of the new approach. We shall not repeat the whole optimization approach; we shall made use of the earlier basic results [2]-[4] derived with the help of optimization procedure from experimental data obtained at irradiation by photons emitted by Co-60 isotope [5].

Assuming the spherical symmetry of corresponding clusters and knowing the diffusion coefficients of individual species (see Table I) the cluster evolution may be characterized by parameter $t$ representing the time having passed from the instant of theoretical diffusion center point origin. It has been then derived in the mentioned optimization procedure that the average initial size of efficient clusters has been cca 20nm, corresponding to the value $t_0 \cong 13$ ns, which represents the proper starting point of average efficient radical cluster evolution how it goes at values $t > t_0$. Average initial numbers of radicals $H^\bullet$, $OH^\bullet$, $e_{aq}^-$, and $H_3O^+$:

$$N_H = 1.3, \; N_{OH} = 17.2, \; N_e = 14.8, \; N_{H_3 0} = 18.8.$$

The time dependencies of individual species concentrations that may by derived when Petri nets have been applied to are shown in Fig. 3 and in Fig. 4 are shown the time dependencies of individual species numbers. The time dependencies of individual species cluster diameters are shown in Fig. 5.

IV. CONCLUSION

It may be seen that OH radicals and aqueous electrons possess the highest initial concentrations that decrease quickly especially for aqueous electrons. Main radiobiological effect is caused surely by OH radicals as it is assumed commonly. The initial increase of H radical may be regarded as interesting being probably in relation to reaction 7 in Table II.

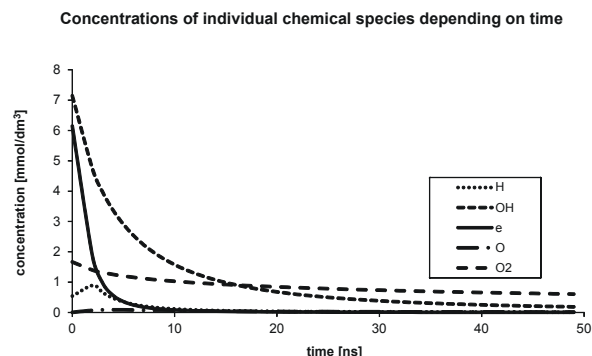The given results correspond to the case when the water has been saturated by oxygen.



Fig. 3 Concentrations depending on time

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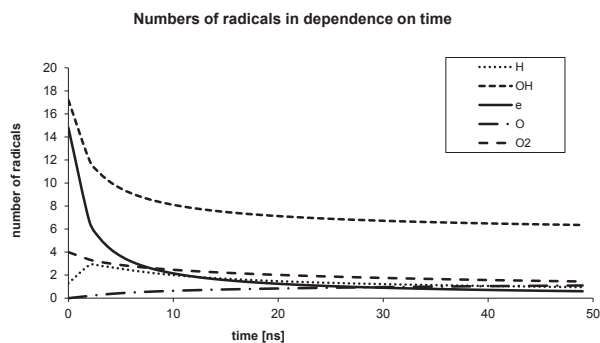International Journal of Bioengineering and Life Sciences
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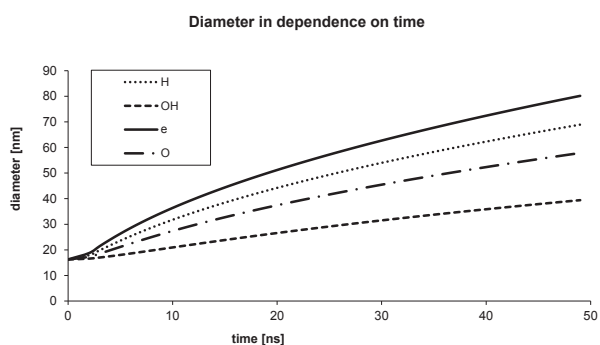Fig. 4 Number of radicals depending on time



Fig. 5 Diameter of cluster depending on time

The presented mathematical model enables us to simulate the chemical stage of the water radiolysis and to obtain the time dependencies of the concentrations of radicals and other species in individual efficient clusters. The Continuous Petri nets make possible to study the concurrent roles of diffusion process and chemical reactions of individual radicals concurrently. The model may be easily extended to involve the influence of other species or radiomodifiers being present (at different concentrations) in water medium during irradiation. It may be very helpful in studying the influence of different stages of radiobiological process on final radiobiological effect in living cells.

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