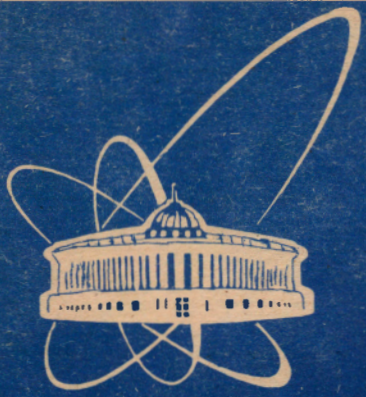

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MATHEMATICAL MODEL OF THE SOS RESPONSE REGULATION IN WILD-TYPE *ESCHERICHIA COLI*

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1 Introduction

Investigation of the physiology and regulation of the SOS response in *Escherichia coli* bacteria during the past decades has revealed the basic features of mechanisms underlying functioning of the SOS system. The system consists of at least 20 unlinked bacterial genes whose products are involved in the SOS response. The basis for the SOS regulation is the specific interaction of two SOS genes *lexA* and *recA*, as demonstrated in various biochemical and genetic experiments [1]. LexA protein functions as a repressor for all SOS genes, including *lexA* and *recA* genes, and RecA protein in an active form (RecA*) stimulates LexA autocleavage reaction. After DNA is damaged following, for example, cell exposure to a typical mutagen ultraviolet (UV) radiation, the SOS-inducing signal is formed which activates RecA for its specific roles in the SOS response. RecA* then accumulates and consequently the LexA concentration drops to the level low enough for increased expression of various SOS genes, thus allowing the introduction of the SOS functions constituting the SOS response. SOS functions serve to recover a cell from the damage. Elimination of the SOS signal results in accumulation of LexA and return of SOS genes to their initially repressed state.

To understand the SOS response regulation a kinetic analysis of regulatory *lexA* and *recA* genes expression after DNA damage is important. Earlier we proposed a model for the SOS response regulation in a *uvr*$^-$ mutant of *E. coli* which is deficient in *uvrABC*-dependent nucleotide excision repair [2]. Excision repair is the major pathway for elimination of pyrimidine dimers (PD) from DNA, the principal type of DNA damage after UV irradiation [3]. While the importance of excision repair in cell recovery from DNA damage was shown in experiments with *E. coli uvr*$^-$ strains [4], the way excision repair modulates SOS regulation is less investigated.

In this paper we propose a means to calculate the level of the SOS signal in wild-type *E. coli* after UV irradiation and show how excision repair affects the kinetics of the SOS signal, and subsequently the expression of the SOS genes. The correlation between excision repair of PDs and SOS signal generation is not obvious because it is not the PDs themselves but rather gaps of single-stranded DNA (ssDNA) opposite PDs that constitute the SOS signal [5]. The simulation of LexA repressor concentration agrees with experimental data and the model is thus verified. We conclude that the essential components of the SOS regulation in wild-type *E. coli* have been modelled and a computational tool developed to be used in investigating quantitative aspects of the SOS response induction in different strains of *E. coli* after virtually any DNA-damaging treatment.

2 The Model

The SOS regulation is based on such an interplay of LexA and RecA proteins as to provide efficient repression of SOS genes under normal growth conditions and to greatly enhance their transcription after DNA damage. It thus appears that coordinated variaton in LexA and RecA intracellular concentrations govern the SOS response induction. To describe the kinetics of the SOS regulation we need to enumerate the cellular events responsible for the observed LexA and RecA dynamics. From the current model for the SOS regulation outlined in the Introduction (see also ref. [1]) we infer that LexA concentration increases through *lexA*-controlled synthesis from the *lexA* locus and decreases through spontaneous and RecA*-mediated breakdown of LexA. RecA concentration increases through *lexA*-controlled synthesis from the *recA* locus and RecA* reversal to its non-active form (RecA), and decreases through RecA transition to the active form and RecA breakdown. Activation of RecA occurs in the reaction with ssDNA that originates in the chromosome after UV irradiation [5, 6]. The formulation of the SOS regulation in terms of these "inflow"/"outflow" events allowed us to write differential equations with respect to LexA, RecA and RecA* concentrations [2]. Using notations C_L, C_R and C_{R*} for these concentrations the differential equations read thus:

$$\frac{dC_L}{dt} = \frac{a_L}{1 + K_L C_L} - b_L C_L C_{R*} - e_L C_L, \tag{1}$$

$$\frac{dC_R}{dt} = \frac{a_R}{1 + K_R C_L} - e_R C_R - b_R C_R C_S + b_{R*} C_{R*}, \tag{2}$$

$$\frac{dC_{R*}}{dt} = b_R C_R C_S - b_{R*} C_{R*}. \tag{3}$$

Here C_S denotes concentration of ssDNA in a cell which is used to measure the level of the SOS signal. Eqns (1–3) describe kinetics of LexA and RecA concentrations in a cell after DNA damage. The specificity of a DNA-damaging treatment is hidden in the function $C_S(t)$, the SOS signal kinetics, and as soon as we somehow know this function we are able to simulate LexA and RecA concentrations. In what follows we will calculate $C_S(t)$ for the case of UV irradiation.

3 Kinetics of the SOS Signal

3.1 Increase in the Level of the SOS Signal

It has been shown previously that the SOS signal originates during replication of a UV-damaged chromosome [5]. It is believed that when the replisome encounters a PD, it disassembles, delays and resumes its movement further on leaving a gap opposite the PD. Indeed, single-stranded defects were detected in an experiment with replicating UV-irradiated *uvrA6* mutant of *E. coli* [7]. The process of gaps generation is schematically shown in Figure 1. Now, the idea is that if we count each PD met by the replisome we will be able to follow the accumulation of ssDNA of gaps. The rate of gaps production is inversely proportional to the period of time required for the formation of one gap (t_G). Thinking this way we obtain the differential equation for the number of gaps formed by t min (N_G):

$$\frac{dN_G}{dt} = \frac{1}{t_G}. \tag{4}$$

Let L be the number of base pairs in the *E. coli* chromosome, and N_0 the number of PDs introduced by a given dose of UV radiation. The value of t_G can be calculated from the delay time, (t_P), and the time required for a replisome to travel between adjacent PDs. Assuming PDs to be distributed uniformly along the chromosome with the average distance between them $\bar{l} = L/N_0$, which is true for $N_0 \gg 1$, we obtain

$$t_G = t_P + \frac{\bar{l}}{v_S}, \tag{5}$$

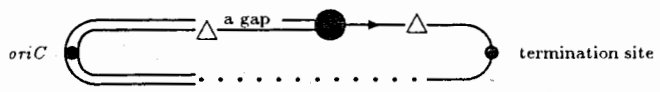

Fig. 1: Scheme for generation of gaps during replication. Two forks proceed from the origin of replication (*oriC*) at identical rates producing gaps at each PD met. *Triangles* denote PDs, *large circle* denotes the fork.

where v_S is the rate of chain elongation by DNA polymerase III. While t_G is constant in case of a uvr^- mutant because of a defect in the PDs' removal system, in a wild-type cell it becomes a function of time. The way excision repair modulates the SOS signal kinetics is in fact by removing a portion of PDs in front of the replication fork, thus reducing PDs' density.

To calculate t_G, let L_r be the distance covered by the replisome by t min. It is determined from the formula

$$L_r = v_S(t - t_P N_G),$$

where $v_S t_P N_G$ accounts for the distance not covered by the replisome because of delay at N_G PDs. The amount of parental DNA to be replicated calculates from L_r as

$$L_{non-r} = \frac{L}{2} - L_r = \frac{L}{2} + v_S(t_P N_G - t). \tag{6}$$

Here $1/2$ in front of L is to account for the fact that the replication is bidirectional [1]. To proceed let us introduce two auxiliary variables: N_E for the number of PDs excised from an unreplicated part of the chromosome, and N_L for the number of PDs left in the unreplicated part of the chromosome and potent to give rise to gaps. Variables N_G, N_E and N_L follow the constraint

$$N_G + N_E + N_L = \frac{N_0}{2}. \tag{7}$$

Assuming the distribution of PDs to remain uniform, the average distance is determined from the formula

$$\bar{l} = \frac{L_{non-r}}{N_L}. \tag{8}$$

[1] Since two replication forks proceed from a single origin of replication at similar rates, it is convenient to perform calculations for one half of the chromosome only, and then multiply the result by two. See Figure 1.

Then, substituting $\bar{l}$, L_{non-r} and t_G from eqns (8), (6) and (5) to eqn (4), we obtain differential equation for N_G in the form

$$\frac{dN_G}{dt} = \frac{N_L}{T_0 + \frac{N_0}{2}t_P - N_E t_P - t}, \tag{9}$$

where $T_0 = L/(2v_S)$ is the length of the C period of the cell cycle when the DNA replication occurs.

Kinetics of excision repair of PDs is to be described by an exponential (36) (see Appendix for derivation). Function (36) in current notation can be rewritten in the form of differential equation

$$\frac{dN_E}{dt} = kN_L. \tag{10}$$

From the constraint (7) and eqns (9–10) we obtain the differential equation for N_L:

$$\frac{dN_L}{dt} = N_L \left[\frac{1}{t_P N_E + t - T_0 - \frac{N_0}{2}t_P} - k \right]. \tag{11}$$

From the biological meaning of N_E and N_L [2] there follow initial conditions for eqns (10–11):

$$N_E(0) = 0, \qquad N_L(0) = \frac{N_0}{2}. \tag{12}$$

Thus, we have to solve eqns (10–11) with initial conditions (12), and use the constraint (7) to obtain $N_G(t)$. The increase in the concentration of ssDNA will then follow the function

$$C_S^{inc}(t) = \frac{2N_G(t)L_G}{N_A V}, \tag{13}$$

where L_G is the average length of a gap, N_A is the Avogadro number and V is an average volume of a bacterial cell.

3.2 Decrease in the Level of the SOS Signal

DNA damage induced in *E. coli* by UV radiation undergoes complex evolution until it is repaired via multiple pathways [8]. Absorpton of UV light

[2] At the moment of irradiation there are no PDs excised, and all of the introduced PDs are in front of the replication fork.

energy results in the formation of PDs (primary lesions). Gaps in daughter strands (secondary lesions) form after replication proceeds past PDs [7]. Decrease in the SOS signal level is due to gaps repair. Repair of gaps can be described formally by the differential equation in the following way. Let $N_R(t)$ be the number of gaps already repaired by t min. The rate of repair is then proportional to the number of intact gaps, which gives us the equation

$$\frac{dN_R}{dt} = v_R(N_G - N_R) \tag{14}$$

with the initial condition

$$N_R(0) = 0, \tag{15}$$

where v_R is the parameter reflecting the gaps repair capacity of a cell. From this it follows that the concentration of ssDNA of gaps will decrease according to the function

$$C_S^{dec}(t) = \frac{2N_R(t)L_G}{N_A V}. \tag{16}$$

Finally, the concentration of ssDNA in a cell is calculated from formulae (13) and (16) as

$$C_S(t) = C_S^{inc}(t) - C_S^{dec}(t) = \frac{2L_G}{N_A V}\left[N_G(t) - N_R(t)\right]. \tag{17}$$

To calculate (17) we need to solve eqns (10–11) and (14), and use the constraint (7).

4 Estimation of Parameters

Parameters of the model include a_L, K_L, b_L, e_L, a_R, K_R, b_R, b_{R*}, e_R, t_P, L_G, k and v_R. We have estimated the majority of these parameters from the experimental data elsewhere [2]. Parameter definitions along with their values are summarized in Table 1. Only two parameters b_{R*} (rate constant of RecA* reversing its active conformation back to RecA), and v_R (rate of repair of gaps) are not available in the experimental literature and are to be fitted.

Initial conditions for eqns (1–3) are $C_L(0) = 2.2 \times 10^{-6}$ M, $C_R(0) = 1.2 \times 10^{-5}$ M and $C_{R*}(0) = 0$. Other constants used in the above equations take the following values: $L = 4.72 \times 10^6$ base pairs (length of a *E. coli* chromosome), $v_S = 5.9 \times 10^4$ base pairs per min (rate of DNA polymerization), $T_0 = 40$ min (duration of a round of replication), $N_A = 6 \times 10^{23}$ mole^{-1} (Avogadro number) and $V = 10^{-15}$ litres (average volume of a *E. coli* cell).

Table 1: Values of model parameters estimated from experimental data

Notation	Definition	Value
a_L	Maximal rate of LexA production[a]	2.9×10^{-6} M min^{-1}
K_L	Binding constant of LexA to *lexA*	5.0×10^7 M^{-1}
b_L	Rate constant of LexA cleavage	5.8×10^4 M^{-1} min^{-1}
e_L	Rate constant of LexA autocleavage	1.2×10^{-2} min^{-1}
a_R	Maximal rate of RecA production[a]	1.7×10^{-5} M min^{-1}
K_R	Binding constant of LexA to *recA*	5.0×10^8 M^{-1}
b_R	Rate constant of RecA activation	3.7×10^5 M^{-1} min^{-1}
e_R	Rate constant of RecA breakdown	1.3×10^{-3} min^{-1}
t_P	Delay time of replisome at a PD	0.17 min
L_G	Average length of a gap	900 nucleotides
k	Rate of PDs' excision repair	0.2 min^{-1}

[a] As is the case for LexA(Def) mutant with total abscence of the locus repression by LexA protein.

5 Non-dimensionalisation of Equations

To perform numerical solution of model differential equations we need to non-dimensionalize the equations. Let us introduce the following dimensionless variables:

$$x = \frac{C_L}{C_L(0)}, \quad y = \frac{C_R}{C_R(0)}, \quad z = \frac{C_{R*}}{C_R(0)},$$
$$s = \frac{C_S}{L/(N_A V)}, \quad \tau = \frac{t}{T_0},$$
$$n_G = \frac{N_G}{N_0/2}, \quad n_R = \frac{N_R}{N_0/2}, \quad n_E = \frac{N_E}{N_0/2}, \quad n_L = \frac{N_L}{N_0/2} \tag{18}$$

and the following dimensionless parameters:

$$k_1 = \frac{a_L T_0}{C_L(0)}, \qquad k_2 = K_L C_L(0), \qquad k_3 = b_L C_R(0) T_0,$$
$$k_4 = e_L T_0, \qquad k_5 = \frac{a_R T_0}{C_R(0)}, \qquad k_6 = K_R C_L(0),$$
$$k_7 = e_R T_0, \qquad k_8 = \frac{b_R L T_0}{N_A V}, \qquad k_9 = \frac{L_G N_0}{L}, \qquad k_{10} = k T_0,$$
$$k_{11} = \frac{t_P N_0}{2T_0}, \qquad A = b_{R*} T_0, \qquad B = v_R T_0. \tag{19}$$

In dimensionless variables (18) model equations read thus:

$$\frac{dx}{d\tau} = \frac{k_1}{1 + k_2 x} - k_3 x z - k_4 x, \tag{20}$$
$$\frac{dy}{d\tau} = \frac{k_5}{1 + k_6 x} - k_7 y - k_8 y s + A z, \tag{21}$$
$$\frac{dz}{d\tau} = k_8 y s - A z, \tag{22}$$
$$\frac{dn_E}{d\tau} = k_{10} n_L, \tag{23}$$
$$\frac{dn_L}{d\tau} = n_L \left(\frac{1}{k_{11}(n_E - 1) - 1 + \tau} - k_{10} \right), \tag{24}$$
$$\frac{dn_R}{d\tau} = B(n_G - n_R), \tag{25}$$
$$n_G = 1 - n_L - n_E, \tag{26}$$
$$s = k_9 (n_G - n_R). \tag{27}$$

Initial conditions for differential equations (20–25) are

$$x(0) = 1, \qquad y(0) = 1, \qquad z(0) = 0,$$
$$n_E(0) = 0, \qquad n_L(0) = 1, \qquad n_R(0) = 0. \tag{28}$$

Values of dimensionless parameters (19) calculated from Table 1 are summarized in Table 2. Parameters k_9 and k_{11} are to be calculated at a given number of PDs, (N_0), and parameters A and B are to be fitted.

Table 2: Values of dimensionless model parameters

Notation	Value	Notation	Value
k_1	52.7	k_7	0.052
k_2	110	k_8	1.16×10^5
k_3	27.8	k_9	$1.91 \times 10^{-4} \cdot N_0$
k_4	0.48	k_{10}	8
k_5	56.7	k_{11}	$2.13 \times 10^{-3} \cdot N_0$
k_6	1100		

6 Results and Discussion

The model formulated above allows simulation of LexA and RecA regulatory proteins kinetics. We have solved the Cauchy problem (20–25) with initial conditions (28) numerically to obtain kinetic curves $x(\tau), \ldots$. Values of model parameters were from Table 2. Values of parameters A and B were determined by a least squares method when fitting simulated $x(\tau)$ to experimental data on LexA concentration kinetics taken from [5]. The dose of UV radiation in the experiment was $D = 5$ J/m^2. The corresponding number of introduced PDs equals $N_0 = 250$ as calculated from the formula $N_0 = 50D$ [7].

Simulated LexA concentration in a cell alongside with experimental data from [5] is shown in Figure 2. One can see that the simulation agrees with experimental data reasonably well. We believe that this agreement validates our model. The last part of the simulated curve seems to disagree with experimental data, however, we do not think that this inconsistence with the data should be attributed to some kind of irrelevancy of our model. This is rather due to inconsistence of the data set used here with some other facts concerning LexA kinetics. Indeed, it has been reported previously that the level of *lexA* mRNA in a cell induced with a similar UV dose tends to decline slowly, reaching its basal level only at 180 min [9]. This finding indicates that LexA protein accumulates relatively slowly as predicted by

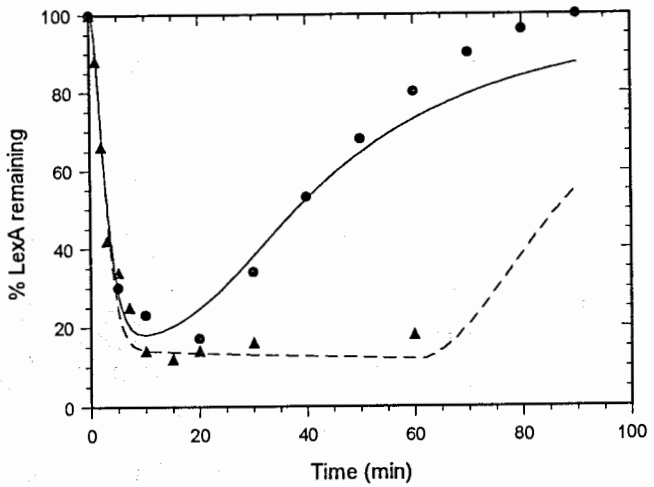

Fig. 2: Simulated LexA concentration in a wild-type (*solid line*) and a uvr^- (*dashed line*) *E. coli* cell after UV irradiation at the dose of 5 J/m^2. Experimental data are shown with symbols: *circles* for wild-type and *triangles* for uvr^- cells.

our simulation. However, to resolve this inconsistence to the endpoint, more research is needed.

To compare LexA kinetics in a wild-type cell to that in a uvr^- cell, we have chosen to show previously simulated in [2] LexA curve for a uvr^- mutant (Figure 2, dashed line). As expected, LexA level stays low until replication terminates at 60 min because no PDs' excision occurs in a uvr^- cell. The effect of excision repair nonfunctionality is in that it lets the prolonged induction of the SOS response to ensure maximum recovery of a cell from the DNA damage. This can also be seen, and more clearly, from the simulation of the SOS signal kinetics, as shown for both wild-type and excision repair deficient cells in Figure 3. In a wild-type cell the concentration of ssDNA increases shortly after UV irradiation to the level of about 12 μM, then decreases relatively quickly and finally disappears by 40 min. In contrast, in a uvr^- cell ssDNA persists for a longer time, as long as the replication of the chromosome takes place. The maximum level of ssDNA is twofold higher (approximately 25 μM). When the replication is over, concentration of ssDNA drops quickly because of DNA repair. Interestingly, the initial rate

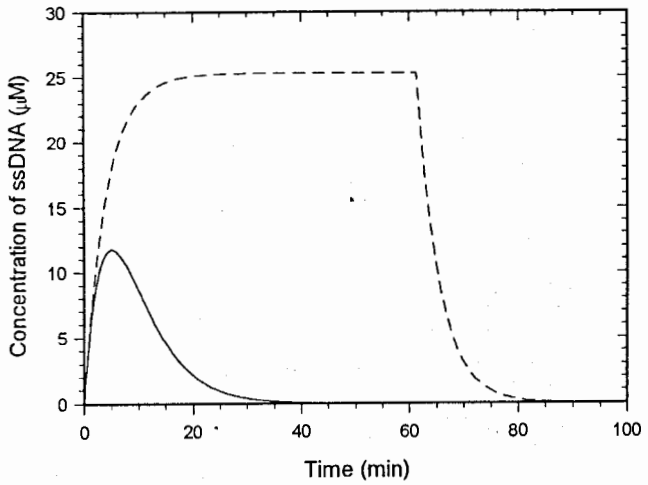

Fig. 3: Simulated concentration of ssDNA in wild-type (*solid line*) and uvr^- (*dashed line*) cells. UV dose is 5 J/m^2.

of ssDNA production is the same in both wild-type and uvr^- cells, implying that excision repair in a wild-type cell does not remove PDs fast enough to modify the rate of the SOS signal production, and consequently RecA activation and LexA cleavage, during the first few minutes of the SOS response. This is consistent with the finding of Sassanfar and Roberts [5] that initial LexA cleavage rates are the same in wild-type and *uvrA* mutant strains.

We conclude that the SOS response is more pronounced and lasts longer in uvr^- mutant than in a wild-type cell because of the lack of excision repair system functionality. Excision repair modulates the SOS response by directly affecting the SOS signal kinetics. It removes PDs in front of the proceeding replication fork, lowering the amount of ssDNA produced and speeding up the SOS response turn-off.

Fitting of LexA kinetic curve to experimental data produced the following values of parameters A and B:

$$A = 150 \pm 40, \qquad B = 10 \pm 2. \tag{29}$$

Calculating dimensional equivalent of A we obtain

$$b_{R*} = 4 \pm 1 \text{ min}^{-1},$$

which corresponds to the half-life of RecA* reversing its activity equal to

$$t_{1/2} = 0.17 \pm 0.04 \text{ min.}$$

The value of $t_{1/2}$ calculated this way does not reflect an intrinsic stability of RecA* protein, but rather is the characteristic of the turn-over of RecA* under specific conditions of SOS induction. At equilibrium RecA unbinds from ssDNA with a half-life of about 30 min [10]. However, in a SOS-induced cell $t_{1/2}$ appears to be much shorter because RecA molecules are displaced from ssDNA when gaps are repaired.

Calculating dimensional equivalent of B we obtain

$$v_R = 0.25 \pm 0.05 \text{ min}^{-1},$$

which is the rate of repair of gaps. This parameter is the characteristic of repair capability of a cell. Interestingly, this value is similar to the rate of PDs removal by excision repair (Table 1).

Concluding, we see that the core of the model [eqns (1–3)] possesses the considerable generality in that the model can be used to describe the SOS response kinetics after *any* DNA-damaging treatment, provided the SOS signal kinetics (function $C_S(t)$) is known. Furthermore, one can add equation(s), similar to eqns (1–2), to describe the kinetics of induction of any SOS gene whose transcription is controlled by LexA. This would allow broader quantitative investigation of expression of various SOS functions. Different mutant strains can in principle be investigated, by simply varying values of appropriate parameters and/or modifying the equations. An example of such an approach is given in our previous work [2], in which we analyzed *uvr*$^-$ and *dnaC*28 mutants. The latter one is a temperature sensitive replication initiation mutant. Analysis of the LexA protein and the SOS signal kinetics in this mutant strain provided insights into the role of DNA replication in the SOS response regulation. One of the SOS functions is the enhanced mutability of the bacterial chromosome. Kinetic analysis of this particular important subset of the SOS response, mediated by products of *recA* and *umuDC* SOS genes, may also be performed with our model.

Appendix: Kinetics of Excision Repair

The mathematical formulation of the problem is as follows. We search for a function $N_{PD}(t)$ describing the kinetics of PDs' removal from a UV-irradiated

bacterial chromosome by excision repair, provided that at the moment $t = 0$ there are $N_{PD}(0) = N_0$ dimers induced by a given dose of UV radiation. Consider stochastic process $Z(t)$ with a denumerable set of states indexed from 0 to ∞. Let us put the number of PDs, (N_{PD}), into correspondence with the state number. The change of the state of the process $Z(t)$ occurs at random times $\tau_1, \tau_2, \ldots$ as a result of PDs' excision. Assume moments $\tau_1, \tau_2, \ldots$ comprise a Poisson fluence with density μ. Let variable $\xi(t)$ be the number of moments τ_k from the interval $[0, t)$. Hence, the probability of transition from a state number n to a state number k is $C_n^k \alpha^{n-k}(1-\alpha)^k$, and the probability to remain in the state number n is $(1-\alpha)^n$, where C_n^k is the binomial coefficient and $0 < \alpha < 1$. Let $P^n(t)$ be the probability for the process $Z(t)$ be in the state number n at a given moment t. The required variable $N_{PD}(t)$ will then be the mathematical expectation of the state number of the process $Z(t)$.

It can be shown that $P^n(t)$ satisfies the following denumerable set of differential equations:

$$\frac{dP^n}{dt} = \mu \left[\sum_{i=0}^{\infty} \left\{ P^{n+i}(t) C_{n+i}^n \alpha^i (1-\alpha)^n \right\} - P^n(t) \right], \qquad n = 0, 1, \ldots \quad (30)$$

with initial conditions

$$P^n(0) = a_n \geq 0, \qquad \sum_{n=0}^{\infty} a_n = 1, \quad (31)$$

where a_n are constants. The problem (30–31) complies with the theorems formulated in [11] from which it follows that there exists the unique, bounded, equicontinual solution of (30–31) determinal at $t \in [0, \infty)$.

In order to find this solution let us introduce the generating function according to the formula

$$\Phi(t, x) = \sum_{n=0}^{\infty} P^n(t) x^n,$$

where $x \in [0, 1]$. Rewriting (30–31) in terms of $\Phi(t, x)$ we obtain the differential equation

$$\frac{\partial \Phi(t, x)}{\partial t} = \mu \left[\Phi(t, (1-\alpha)x + \alpha) - \Phi(t, x) \right] \quad (32)$$

with the initial condition

$$\Phi(0,x) = \sum_{n=0}^{\infty} a_n x^n \tag{33}$$

and boundary condition

$$\Phi(t,1) = 1. \tag{34}$$

The solution of eqn (32) with initial and boundary conditions (33) and (34) follows in the form of a series of functions:

$$\Phi(t,x) = e^{\mu t} \sum_{k=0}^{\infty} \sum_{n=0}^{\infty} a_n \frac{t^k \mu^k}{k!} \left[1 + (1-\alpha)^k (x-1)\right]^n. \tag{35}$$

The mathematical expectation for the problem (30–31) is defined as $M(t) = \partial\Phi/\partial x|_{x=1}$. Differentiating (35) with respect to x according to this definition and letting $x = 1$, we obtain

$$M(t) = M(0) e^{-\alpha\mu t}.$$

Coming back to the number of PDs we see that it decreases with time following the exponential:

$$N_{PD}(t) = N_0 e^{-kt}, \tag{36}$$

where $k = \alpha\mu$ is the rate of pyrimidine dimers excision.

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Математическая модель регуляции SOS-ответа бактерий *Escherichia coli* дикого типа

Регуляция SOS-ответа бактерий *Escherichia coli*, представляющего собой набор индуцибельных клеточных реакций, проявляющихся после повреждения ДНК, происходит в результате особого взаимодействия белков LexA и RecA. LexA-белок является общим репрессором генов SOS-системы, а RecA-белок, будучи активирован в реакции с SOS-индуцирующим сигналом, ускоряет реакцию спонтанного расщепления LexA-белка. Ранее мы описали регуляцию SOS-системы при помощи дифференциальных уравнений относительно концентраций белков LexA и RecA. Входной функцией к уравнениям модели является зависимость уровня SOS-сигнала от времени. В настоящей работе предлагается модель для расчета концентрации однонитевой ДНК (SOS-сигнала) как функции времени в клетках дикого типа после ультрафиолетового облучения. Используя уравнения модели, можно рассчитывать кинетические кривые регуляторных SOS-белков после повреждения ДНК с целью изучения кинетики SOS-ответа. Расчет кинетической кривой LexA-белка согласуется с экспериментальными данными. В работе проведено сравнение расчетных кинетических кривых LexA-белка у бактерий дикого типа и *uvr*$^-$-мутанта, что представляется полезным при исследовании роли *uvrABC*-зависимой эксцизионной репарации в формировании кинетики SOS-ответа. Обсуждается возможное применение модели к исследованию различных проявлений индукции SOS-ответа.

Работа выполнена в Отделении радиационных и радиобиологических исследований ОИЯИ.

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Mathematical Model of the SOS Response Regulation in Wild-Type *Escherichia coli*

Regulation of the SOS response in *Escherichia coli*, which is a set of inducible cellular reactions introduced after DNA damage, is due to specific interaction of LexA and RecA proteins. LexA protein is a common repressor of the genes of the SOS system, and RecA protein, once transiently activated by the so-called SOS-inducing signal, promotes LexA protein destruction. We have described the SOS regulation by means of differential equations with regard to LexA and RecA concentrations elsewhere. The «input» function for model equations is the level of the SOS-inducing signal against time. Here we present a means for calculating the concentration of single-stranded DNA (SOS-inducing signal) as a function of time in wild-type cells after ultraviolet irradiation. With model equations one can simulate kinetic curves of SOS regulatory proteins after DNA damage to survey the SOS response kinetics. Simulation of LexA protein kinetics agrees with experimental data. We compare simulated LexA kinetic curves in wild-type and *uvr*$^-$ mutant bacteria, which is useful in investigating the way *uvrABC*-dependent excision repair modulates the SOS response kinetics. Possible applications of the model to investigating various aspects of the SOS induction are discussed.

The investigation has been performed at the Division of Radiation and Radiobiological Research, JINR.

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