Evolution and Mutation Physics

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1. Introduction

In a previous publication [1] the author described the base rivalry in monotonous DNA sequences and their effect on the DNA repair mechanism. As described in the article, during the monotonous sequence replication, energies appear theoretically to increase with a progressive replication fork up to the quantum mechanical energy level n=2 because of the base rivalry, and these rivalry energies affect the bond strength between the complementary bases. If there is a tautomeric base pair in the replication position where the rivalry energy is large enough, then in this position an irreparable mutation will occur, since the DNA repair mechanism cannot repair that error because too much binding energy.
Thus a mutation (caused by base rivalry) can occur only on condition that a transition of a base pair into its tautomeric form is happened . It is remarkable that this transition likewise can occur by the effect of base rivalry energy.
The base rivalry - energy which has an effect on a normal base pair provokes a tunnel process in its hydrogen bond, and produces the tautomeric form. After whose replication a different, irreparable base pair develops from the tautomeric base pair, when the rivalry - energy leads into a very strong hydrogen bond. This happens, however, by chance and in the following we will compute the probabilities of such accidental events. We take as object only a small replication unit (“residual fragment”) because it has a larger probability of such events. The result of these calculations is the equation (32) which could be useful for the theory of evolution and besides for clearing up of virus mutations.

2. The problems

The replication of large DNAs takes place by simultaneous replications of so called replicons with a length of more than 10^4 bp. This happens continuously 5’ -> 3’ on the leading strand and discontinuously on the lagging strand in segments of 100 bp (eucariotic DNA) in the direction 3’ -> 5’. These segments (Okazaki-fragments) are replication units. When the replication of the whole replicon has finished, remains for the present on the lagging strand a small rest (s. fig. 1) which only after the last Okazaki – fragment is replicated. The length of this rest called “residual fragment” may be 0 … 100 bp (eucariotic DNA), and this is also a replication unit because it has a replication beginning and a replication end.

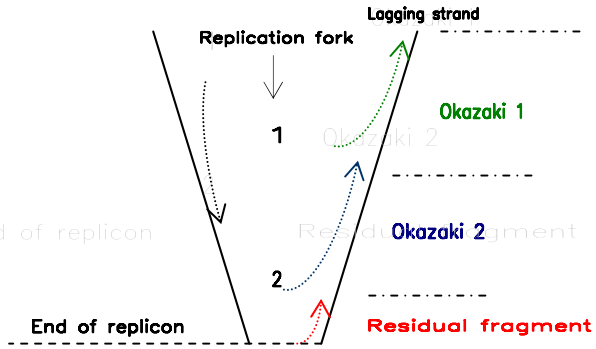

Fig. 1: Schematic specification of replication at end of replicon

Now we assume that in this residual fragment a long monotonous sequence GGGGGGATTA develops in 3'->5' on lagging strand during replication. So, high base rivalry energy comes into being.
To make this clear, let us look to fig 2 where only the small rest of replicon, the residual fragment is shown: One sees the base pair A - T at position 7 (fig. 2a). If the base rivalry energy is large enough (caused by replication of the long monotonous sequence GGG …) then it provokes a tunnel process (s. section 3) transforming the base pair A – T into its tautomeric base pair A* - T* (fig. 2b). Soon after (almost at the same time) a base component dGTP, having the high base rivalry energy, replaces the base A* so that the new base pair G – T* develops (fig. 2c) and this cannot be repaired because of the high binding energy developed between the two bases G and T*. Thus an irreparable mutation arises. We will see that the probability for emergence of high base rivalry energy is the greater, the smaller the residual fragment. The problem of distribution-probability in a sequence appears here (s. section 4).
During the replication after next, the base pair G – T* which has an unusual geometry is transferred into the "perfect wrong" base pair G – C, so that the irreparable mutation is perfect and *the monotonous sequence has lengthened.*

It seems to be interesting, to combine both proceedings: The distribution process which produces the high base rivalry

energy, and the tunnel process which produces the tautomeric base pair. These problems will be examined in section 5.

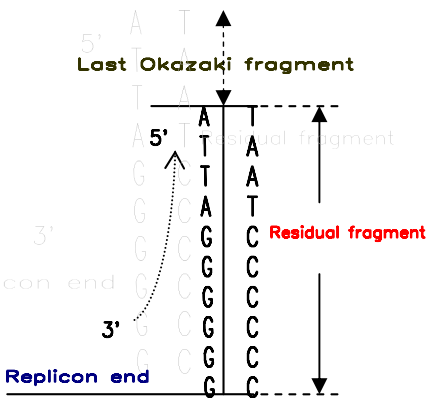

Fig. 2a: Replicating residual fragment before tunneling

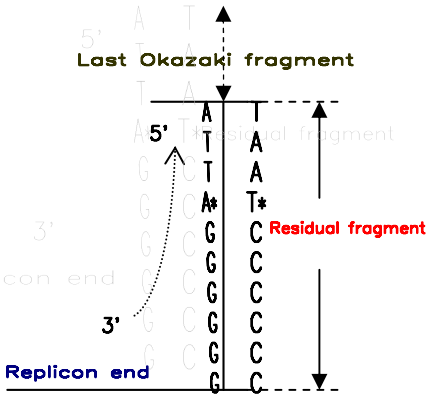

Fig 2b: Replicating residual fragment under tunnel influence

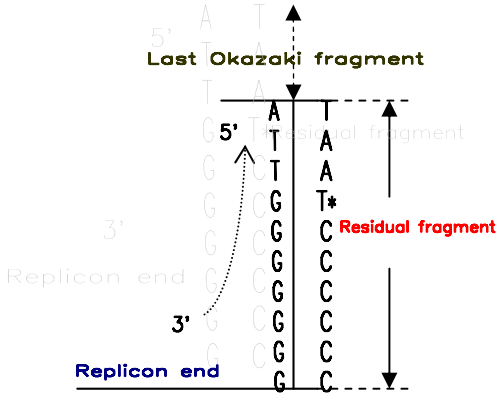

Fig. 2c: Replicating residual fragment after tunnelling; base A* is replaced by the high-energy-base G

In the following, we will describe the 3 phenomena: The tunnel probability (section 3), the distribution probability (section 4), and the combination of both phenomena (section 5).

3. Tunnel processes in biological hydrogen bonds

Figure 3 shows the participating energies, energy of the donor and potential energy of the potential wall in a hydrogen bond. The energy E_{k+1}=(ground state energy)+T_k required for the provocation of the tunnel process is composed of the ground state energy -13.656 eV and the rivalry energy T_k which is created in fig. 2 up to the replication position 6. Therefore, the length of the new monotonous sequence is one position larger than the position k, where the rivalry energy in accord with the formula

$$T_k = k\left(\frac{e_0^2}{r_1} - \frac{e_0^2}{r_B}\right) - z\cdot\sqrt{\frac{e_0^2}{r_1} - \frac{e_0^2}{r_B}} \qquad (1)$$

arises (see [1]). (e_0 = elementary charge, r_1 = distance between the related complementary bases, r_B = distance between successive bases, z is specific value based on the viscosity of the nucleoplasm.

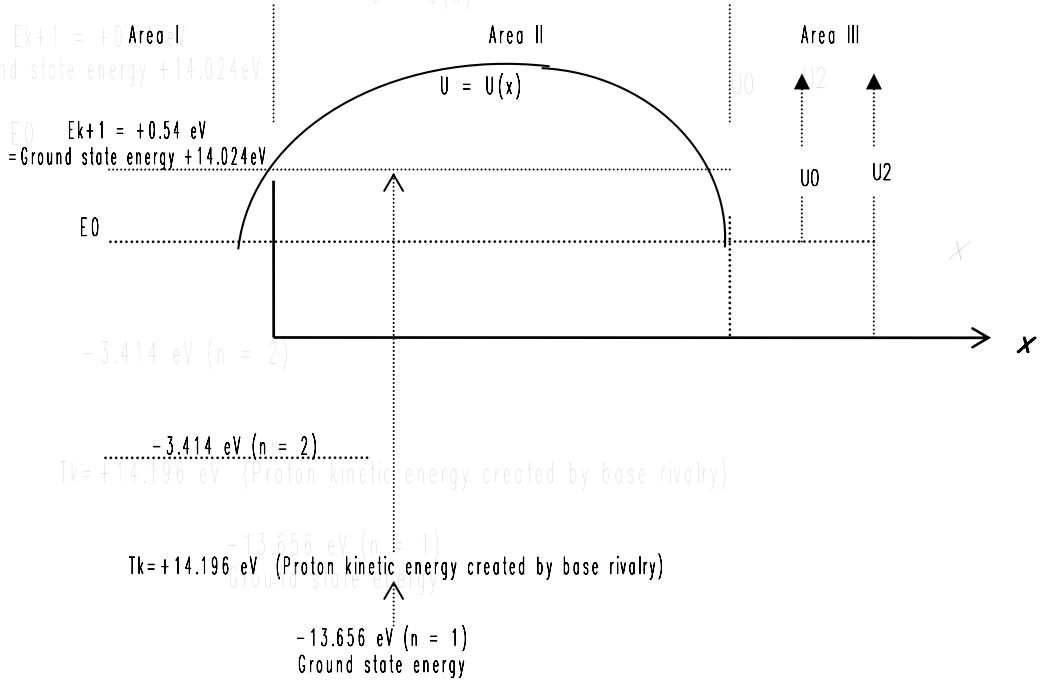

Figure 3 shows the energy levels, which the donor of a hydrogen bond passes because of the base rivalry, and the energies of the potential wall of the hydrogen bond:

While the energy in the quantum mechanic energy level n = 1 is -13,656 eV (ground state energy), the donor of the hydrogen bond receives the energy T_k, which is, for example +14,196 eV. This gives the donor the total energy -13,656 +14,196 = + 0,54 eV and reaches an energy that is not only over the energy level n = 2 (-3,414 eV), but extends into the potential field of hydrogen bond and thus provokes a tunnel passage.

3.1. The tunnel probability

How large is the probability of the tunnel passage of a proton through the potential wall? The calculation of the number of the protons passing through the potential wall in biological hydrogen bonds has been carried out for the first time by P. Ö. Löwdin [2], the calculation is carried out down to the last detail in [3]. The result is available for the areas I,

II and III (before, within and behind the potential wall). The three wave equations of the proton are

$$\psi_I(x) = A_1 e^{ik_0 n_1 x} + B_1 e^{-ik_0 n_1 x}$$

$$\psi_{II}(x) = \frac{\alpha}{\sqrt{k_r(x)}} e^{+K} + \frac{\beta}{\sqrt{k_r(x)}} e^{-K}$$

$$\psi_{III}(x) = A_3 e^{ik_0 n_3 x}$$

with

$$k_0 n_1 = \frac{1}{\hbar}\sqrt{2m(E - U_1)}$$

$$k_0 n_3 = \frac{1}{\hbar}\sqrt{2m(E - U_3)}$$

$$\hbar = \frac{h}{2\pi}$$

where h is Planck's constant, and m is the proton mass. Considering the boundary conditions

$$\psi_I(0) = \psi_{II}(0)$$

$$\psi_I'(0) = \psi_{II}'(0)$$

$$\psi_{II}(l) = \psi_{III}(l)$$

$$\psi_{II}'(l) = \psi_{III}'(l)$$

all the constants in the equations (1) can be calculated. As a result, we need only the amplitude A_3 of the proton wave that comes through the wall and the amplitude A_1 of the proton wave approaching to the wall:

$$P = \frac{|A_3|^2}{|A_1|^2} = e^{-2K} = e^{-\frac{2}{\hbar}\int_0^l \sqrt{2m(U-E)}dx} \qquad (2)$$

This is the probability of a single proton tunnelling through the wall. l is the width of the potential wall between the positions, where the tunnel energy E has its smallest level E_0, considering that the tunnelling takes place above of this level. When the temperature t is taken into account, in which the tunnel process is provoked, the "temperature – dependent tunnel - probability" is

$$P_t = e^{-\frac{E}{k_B t} - 2K} \qquad (3)$$

.

k_B is Boltzmann's constant. If the potential wall has the shape of a parabola, then

$$P_t = \exp\left[-\frac{U_2 - E}{k_B t\, t_0}(t - t_0) - \frac{U_2}{k_B t}\right] \qquad (4)$$

where U_2 = peak potential of the wall and the "characteristic temperature"

$$t_0 = \frac{h}{l \cdot \pi^2 k_B} \sqrt{\frac{U_0}{2m}} \qquad (5)$$

U_0 is the height of the wall; m is the proton mass. For the size of U_0, see [4], [5], [6].

$$E = -13.656 \text{ eV} + T_{k-1}$$

is the energy created by base rivalry up to the replication position k-1 when k means the mutation position.

3.2. The change in the tunnel probability due to temperature - and energy - change

We now consider two different tunnel processes. The first operation took place at a hydrogen bond where the potential wall peak value was U_{21}, and the second operation takes place at a hydrogen bond, where the potential wall peak value is U_{22}. In the first process, the energy E_1 operated on the donor at the temperature t_1. In the second process, the energy E_2 operates on the donor at temperature t_2.
For the operations 1 and 2 apply the equations for the tunnel probabilities:

Operation 1: $$P_1 = \exp\left[-\frac{U_{21} - E_1}{k_B t_1 t_{01}} (t_1 - t_{01}) - \frac{U_{21}}{k_B t_1} \right] \qquad (6)$$

and

Operation 2: $$P_2 = \exp\left[-\frac{U_{22} - E_2}{k_B t_2 t_{02}} (t_2 - t_{02}) - \frac{U_{22}}{k_B t_2} \right]. \qquad (7)$$

E_0 = Smallest tunnel energy in the computation
U_{21} = vertex of the potential of the hydrogen bond 1
U_{22} = vertex of the potential of the hydrogen bond 2
t_{01} = characteristic temperature of the hydrogen bond 1
t_{02} = characteristic temperature of the hydrogen bond 2
t_1 = temperature during Operation 1
t_2 = temperature during operation 2
E_1 = total energy of a proton before tunnel process in the operation 1
E_2 = total energy of a proton before tunnel process in the operation 2

$$k' = \frac{2m\pi^4 l^2 k_B^{\,2}}{h^2} = 4.9738 \cdot 10^{-6}\ eV \cdot grad^{-2}$$

$k_B = 0.863 \cdot 10^{-4}\ eV \cdot grad^{-1}$ Boltzmann's constant

The ratio of the tunnel probabilities is

$$\frac{P_2}{P_1} = \exp\left\{ -\frac{U_{22} - E_2}{k_B t_2 t_{02}} (t_2 - t_{02}) - \frac{U_{22}}{k_B t_2} + \frac{U_{21} - E_1}{k_B t_1 t_{01}} (t_1 - t_{01}) + \frac{U_{21}}{k_B t_1} \right\}$$

$$= \exp\left\{ \frac{1}{k_B t_1} \left[(U_{21} - E_1) \frac{t_1 - t_{01}}{t_{01}} + U_{21} \right] - \frac{1}{k_B t_2} \left[(U_{22} - E_2) \frac{t_2 - t_{02}}{t_{02}} + U_{22} \right] \right\}$$

$$= \exp\left\{ \frac{1}{k_B t_1} \left[U_{21} \cdot \frac{t_1}{t_{01}} - E_1 \left(\frac{t_1}{t_{01}} - 1 \right) \right] - \frac{1}{k_B t_2} \left[U_{22} \frac{t_2}{t_{02}} - E_2 \left(\frac{t_2}{t_{02}} - 1 \right) \right] \right\}$$

$$= \exp\left\{ \frac{1}{k_B\, t_1}\left[U_{21} \cdot \frac{t_1}{t_{01}} - E_1 \frac{t_1}{t_{01}} + E_1 \right] - \frac{1}{k_B\, t_2}\left[U_{22} \frac{t_2}{t_{02}} - E_2 \frac{t_2}{t_{02}} + E_2 \right] \right\}$$

$$\frac{P_2}{P_1} = \exp\left\{ \frac{1}{k_B\, t_1}\left[U_{21} \cdot \frac{t_1}{t_{01}} - E_1 \frac{t_1}{t_{01}} \right] + \frac{E_1}{k_B\, t_1} - \frac{1}{k_B\, t_2}\left[U_{22} \frac{t_2}{t_{02}} - E_2 \frac{t_2}{t_{02}} \right] - \frac{E_2}{k_B\, t_2} \right\} \qquad (8)$$

Using the abbreviation

$$\Delta_S = \frac{E_2}{t_2} - \frac{E_1}{t_1} \qquad (9)$$

one gets

$$\frac{P_2}{P_1} = \exp\left\{ \frac{1}{k_B\, t_1}\left[U_{21} \cdot \frac{t_1}{t_{01}} - E_1 \frac{t_1}{t_{01}} \right] - \frac{1}{k_B\, t_2}\left[U_{22} \frac{t_2}{t_{02}} - E_2 \frac{t_2}{t_{02}} \right] - \frac{1}{k_B} \Delta_S \right\}$$

$$\frac{P_2}{P_1} = \exp\left\{ -\frac{1}{k_B\, t_{02}}\left[U_{22} - E_2 \right] + \frac{1}{k_B\, t_{01}}\left[U_{21} - E_1 \right] - \frac{1}{k_B} \Delta_S \right\} \qquad (10)$$

According to fig. 3:

$$U_{22} = U_{02} + E_0$$

$$U_{21} = U_{01} + E_0 \qquad (11)$$

$$\frac{P_2}{P_1} = \exp\left\{ -\frac{1}{k_B\, t_{02}}\left[U_{02} + E_0 - E_2 \right] + \frac{1}{k_B\, t_{01}}\left[U_{01} + E_0 - E_1 \right] - \frac{1}{k_B} \Delta_S \right\} \qquad (12)$$

From eq.(5):

$$U_{01,02} = k' t_{01,02}^{\,2}$$

$$\frac{P_2}{P_1} = \exp\left\{ -\frac{1}{k_B\, t_{02}}\left[k' t_{02}^2 + E_0 - E_2 \right] + \frac{1}{k_B\, t_{01}}\left[k' t_{01}^2 + E_0 - E_1 \right] - \frac{1}{k_B} \Delta_S \right\}$$

$$\frac{P_2}{P_1} = \exp\left\{ -\frac{1}{k_B}\left[k' t_{02} \right] + \frac{1}{k_B}\left[k' t_{01} \right] - \frac{E_0 - E_2}{k_B\, t_{02}} + \frac{E_0 - E_1}{k_B\, t_{01}} - \frac{1}{k_B} \Delta_S \right\}$$

$$= \exp\left\{ + \frac{1}{k_B}\left[k'\left(t_{01} - t_{02} \right) + \frac{t_{02} E_0 - t_{02} E_1 - t_{01} E_0 + t_{01} E_2}{t_{01}\, t_{02}} - \Delta_S \right] \right\}$$

$$\frac{P_2}{P_1} = \exp\left\{ + \frac{1}{k_B}\left[k'\left(t_{01} - t_{02} \right) - \frac{t_{02} E_1 - t_{01}\left(\Delta E_2 + E_1 \right) - E_0\left(t_{02} - t_{01} \right)}{t_{01}\, t_{02}} - \Delta_S \right] \right\}$$

With the abbreviations

$$\Delta E_1 = E_1 - E_0$$

$$\Delta E_2 = E_2 - E_1 \qquad (13)$$

$$\Delta_C = \frac{E_2}{t_0} - \frac{E_1}{t_0} \qquad (14)$$

resulting in

$$\frac{P_2}{P_1} = \exp\left\{ + \frac{1}{k_B}\left[k'\left(t_{01} - t_{02} \right) - E_1 \frac{t_{02} - t_{01}}{t_{01}\, t_{02}} + \frac{\Delta E_2}{t_{02}} + E_0 \frac{t_{02} - t_{01}}{t_{01}\, t_{02}} - \Delta_S \right] \right\} \qquad (15)$$

$$\frac{P_2}{P_1} = \exp\left\{ + \frac{1}{k_B}\left[k'\left(t_{01} - t_{02}\right) + \frac{\Delta E_2}{t_{02}} - \frac{\Delta E_1}{t_{01}} \frac{t_{02} - t_{01}}{t_{02}} - \Delta_S \right]\right\} \qquad (16)$$

Assuming that two consecutive tunnel operations always work on the *same type* of binding and therefore $t_{01}=t_{02}=t_0$, then

$$\left(\frac{P_2}{P_1}\right)_{t_{01}=t_{02}} = \exp\left\{\frac{1}{k_B}\left[\Delta_C - \Delta_S\right]\right\} \qquad (17)$$

This is the proportion of a second tunnel process probability to a first tunnel process probability where both processes take place at different energies and temperatures. In each case of tunnelling, a tautomeric base pair is created. After replication in each process a different base pair develops from the tautomeric base pair which is inseparable, if a high rivalry energy led to an inseparable hydrogen bond. So the DNA repair mechanism is ineffective, and the base distribution changes irreparably in each of the two proceedings.
Let us now, for the present irrespective of energies and temperatures examine *statistically* the distribution changes in DNA-fragments. We shall come back to the equations (16) and (17) later in section 5.

4. The distribution of bases on the DNA during replication, and the chance of occurrence of high base rivalry energy

In this section, the distribution change is examined from the point of view of an observer which does not know the physical equations (6) and (7) but only knows that a monotonous sequence lengthening appears sometimes during replication. The observer calculates the prospects of a base component to reach that place where the lengthening occurs, provided that the ticket for that place during replication is decided by drawing lots.
During the replication of a certain DNA-segment, a distribution of all base components takes place which are produced in the cell onto the codogen matrix. This happens in accordance with the copy rule. In this distribution, some base components are exposed to the base rivalry (if they get to a monotonous sequence) but others not. Those produced base components which are exposed to the base rivalry respond in very different ways: Most of them lose their obtained energy owing to deviation, friction or owing to short fading times. Only a few are scarcely deflected, or have long fading times. Even fewer base components still have so much energy at the end of the base rivalry (that is, at the end of the monotonous sequence replication) that they provoke a tunnelling in the next replication position and can build an irreparable hydrogen bond because their donor energy is still over the quantum mechanical energy level n = 2.

It is assumed that *any given base component only accidentally* will possess the ability to reach and to maintain a high energy level because exact properties of a base component produced in the cell cannot be identified. However, there will be one of all base components produced in the cell which best joins those qualities (to reach and to maintain a high energy) together in itself. We name this base component the *"elitist component".*
This section lists all the favourable and all possible distributions within the certain DNA-segment. The favourable distributions are those in which the elitist component accidentally arises there where the base rivalry works. The proportion of the number of the favourable distributions to the number of all possible distributions is the appearance probability of the elitist component at this place where the base rivalry works during the DNA – replication.

4.1. Enumeration of all possible distributions
The 4 bases A, C, G, T are represented by the terms *C, S, X, Y. C* is the **c**oncerned base, which in case of a mutation process will be replaced with an irreparable mutation by the **s**ubstituting base *S*. *X* and *Y* are any bases which do not change in the distribution change.

For the purpose of simplification, we look at only one base type e.g. the base type *S* in fig. 4. In the case of fig. 4 the copy – instruction requires that in the first monotonous sequence two identical bases *S,S,* in the second "monotonous" sequence one base S, and in the third monotonous sequence three identical bases *S,S,S* must exist.

Origin base sequence:

X	*S*	*S*	*C*	*X*	*Y*	*X*	*Y*	*Y*	*C*	*S*	*C*	*Y*	*C*	*X*	*X*	*S*	*S*	*S*	*Y*	*Y*	*X*

Split base sequence:

	S	*S*								*S*						*S*	*S*	*S*			
X				*X*		*X*								*X*	*X*						*X*
			C						*C*		*C*		*C*								
					Y		*Y*	*Y*				*Y*							*Y*	*Y*	

Figure 4: base sequence split into sequences of equal bases.

How large is the number of possibilities to distribute itself as in fig 4 (agreeing with the copy – instruction)? Because all S-bases belong to the same base type, each base of the one monotonous sequence can accidentally appear in another monotonous sequence of the same base type. The enumeration of

all possible cases to distribute itself in the base type *S* as in fig. 4 results in

$$\frac{6!}{2!1!3!} = 60$$

This is the same as in a classroom with 10 students, where by the teacher's direction the students distribute themselves on 2 benches containing four students each and 1 bench containing only two students. How the students arrange themselves is irrelevant to the teacher. There are $\frac{10!}{4!\cdot 4!\cdot 2!} = 3150$ various outcomes for the way the teacher has directed the distribution.

In a group of 7 students which are to distribute to 1 bench with 4 students and 1 bench with 3 students, there are 7!/4!/3! = 35 possibilities.

It is important to note that the replication is an establishment of an unchanged copy, only that the base components of a large stock are distributed randomly, but still according to the copy rule.

Designating the total number of the bases *S* as s, the total number of the bases *C* as c, the total number of the bases *X* and *Y* as x and y respectively, and further the number of bases which are located in the single monotonous sequences as

$s_1, s_2, s_3, ..., c_1, c_2, c_3, ..., x_1, x_2, x_3, ..., y_1, y_2, y_3, ...$

(in fig. 4 is $s_1 = 2, s_2 = 1, s_3 = 3$),

then the enumeration of all possible distributions agreeing to the copy –instruction in fig. 4 results in

$$r_1 = \frac{s!}{s_1!s_2!s_3!...} \cdot \frac{c!}{c_1!c_2!c_3!...} \cdot \frac{x!}{x_1!x_2!x_3!...} \cdot \frac{y!}{y_1!y_2!y_3!...} \qquad (18)$$

and the number of all possible distributions in a sequence that is different from the 1. sequence only in the fact that in a box *C* the base number decreased by one, but in the box *S* the base number was increased by one, is

$$r_2 = \frac{(s+1)!}{(s_1+1)!s_2!s_3!...} \cdot \frac{(c-1)!}{(c_1-1)!c_2!c_3!...} \cdot \frac{x!}{x_1!x_2!x_3!...} \cdot \frac{y!}{y_1!y_2!y_3!...} \qquad (19)$$

With both equations, the number of all accidental possible distributions which agree with the copy – instruction is written down. All these distributions can appear during replication.

4.2. Enumeration of all favourable distributions, and the chance of occurrence of high base rivalry energy

Now we wish to know how often an elitist component appears in all these r distributions within a certain monotonous sequence.

To make this clear we take once again the second example of the students: We ask how often one of the 7 students (the "elitist component") in 35 distributions will sit in the bench

with four seats. This student may have the number 1. There are the following versions:

```
1 2 3 4             1 4 5 6
1 2 3 5             1 4 5 7
1 2 3 6             1 4 6 7
1 2 3 7
1 2 4 5             1 5 6 7
1 2 4 6
1 2 4 7
1 2 5 6
1 2 5 7
1 2 6 7

1 3 4 5
1 3 4 6
1 3 4 7
1 3 5 6
1 3 5 7
1 3 6 7
```

The student with the number 1 (the elitist component) can sit

$$1+\sum_{1}^{2}+\sum_{1}^{3}+\sum_{1}^{4}=20$$

times within 35 accidental distributions on the four seat bench, giving the probability 20/35 = 57%. One can take any one number from 1 to 7; the number 20 of all favourable distributions remains the same. We designate the number of all favourable distributions (that is the number of all cases in which the elitist accidentally appears within a monotonous sequence with the length s_1) as σ_{s1} and the number of cases in which the elitist accidentally appears within a monotonous sequence with the length s_1+1 as σ_{s1+1}.

To determinate the number of cases in which a certain base component (the elitist component) while distribution of all s-components accidentally appears *within the six-digit* monotonous sequence we use the step-by-step- program SIGMA6, to find in the web-side:

http://www.basenkon.com/SIGMA.pdf

Then the monotonous sequence is lengthened for one position through the base rivalry so that the length of the monotonous sequence becomes 7 nucleotides. To determinate the number of cases in which the elitist component accidentally is located *within the seven-digit* monotonous sequence we use the step-by-step-program SIGMA7, to find in the same web-side.

The *probability* that an elitist component appears in an s_1-digit monotonous sequence during replication (of whole residual fragment) is

$$W_{s1}=\frac{\sigma_{s1}\cdot r_c\cdot r_x\cdot r_y}{r_1} \qquad (20)$$

where

$$r_c = \frac{c!}{c_1! \cdot c_2! \cdot \ldots}$$

$$r_x = \frac{x!}{x_1! \cdot x_2! \cdot \ldots}$$

$$r_y = \frac{y!}{y_1! \cdot y_2! \cdot \ldots}$$

are the numbers of all possible c-, x-, y- distributions and $r_{1(2)}$ is the number of all possible distributions. This is because that the convenient case (that means, the elitist is within the s_1-digit monotonous sequence) also can appear in each of the c-, x-, y-distributions. The statistical propability that an elitist component appears in an (s_1+1)-digit monotonous sequence during replication is

$$W_{s1+1} = \frac{\sigma_{s1+1} \cdot r_{c-1} \cdot r_x \cdot r_y}{r_2} \qquad (21)$$

$$r_{c-1} = \frac{(c-1)!}{(c_1-1)! \cdot c_2! \cdot \ldots}$$

$$\frac{r_c}{r_{c-1}} = \frac{c}{c_1} \qquad (22)$$

$$\frac{W_{s1+1}}{W_{s1}} = \frac{\sigma_{s1+1}}{\sigma_{s1}} \frac{r_{c-1} \cdot r_1}{r_c \cdot r_2} \qquad (23)$$

Defining the fraction $\frac{\sigma_{s1+1}}{\sigma_{s1}}$ as σ:

$$\frac{W_{s1+1}}{W_{s1}} = \sigma \frac{r_{c-1} \cdot r_1}{r_c \cdot r_2} \qquad (24)$$

Dividing equation (18) through equation (19) results in

$$\frac{r_1}{r_2} = \frac{c}{s+1} \cdot \frac{s_1+1}{c_1} \qquad (25)$$

By inserting (22) and (25) into (24):

$$\frac{W_{s1+1}}{W_{s1}} = \sigma \cdot \frac{s_1+1}{s+1} \qquad (26)$$

s is the total number of the substituting base type *S*. s_1 is the base number in the monotonous sequence which is lengthened in case of mutation. σ depends on the length of the DNA – fragment.

Now we have calculated the probability for a distribution, in which the elitist appears there where the base-rivalry energy becomes highest (in the monotonous sequence sss . . .). On condition that at the end of this monotonous sequence exists a tautomeric base pair then an irreparable mutation develops itself.

Here we will calculate the distribution-probability W_7 for the elitist's appearance in different lengths of residual fragments:

Table 1: Examples of residual fragments

$$W_7 = \frac{\sigma_7 \cdot r_{c-1} \cdot r_x \cdot r_y}{r_2}$$

Resid.-Fragm.	W_7
GGGGGGGATT	1.0
GGGGGGGATTGG	0.78
GGGGGGGATTGGGG	0.64
GGGGGGGAACGTACA	0.875
GGGGGGGATTTAACCCGGTT	0.778
GGGGGGGATTCCCAATTGTAGGCCC	0.233
GGGGGGGGACTTTAAAGGCCATTGCATTGGAACTTG	0.003
GGGGGGGACTTTAAAGGCCATTGCATTGGAACTTGGGGGGGGACTTTAAAGGCCATTGCATTGGAACTTG	1.4×10^{-12}

The substituting base is the base G
The concerned base is the base A
The X-base is the base C
The Y-base is the base T
The calculation of distribution-lots follows by $x!/(x_1!x_2!\ \ldots)$,for example. r_2 must be calculated over all bases.

It is evident that the elitist-appearance-probability W_7 is the smaller, the larger the residual fragment.

5. The total probability of mutation which is caused by base rivalry.

Now it seems to be interesting to combine both tunnel probability and elitist probability.
Two possible processes can occur during replication of a monotonous sequence:
1. A tunnel process (probability P_t) creates a tautomeric base pair (A*-T*) at the end of the monotonous sequence because of high base rivalry energy.
2. The elitist comes (with the probability W_{s1}) into the monotonous sequence. Then, the elitist (G) replaces the base A*, and the binding - energy between the new complementary bases increases itself because of high energy of the elitist and so causes an irreparable base modification (s. fig. 2c).
So the total probability for an irreparable mutation (caused by base rivalry) at the end of an s_1-digit monotonous sequence is the product of tunnel-probability and elitist-probability:

$$\varpi = P_1 \cdot W_{s1} = P_2 \cdot W_{s1+1} \qquad (27)$$

This means that nature works in the following way: The larger the statistical probability at which the preconditions of events occur accidentally, the smaller the physical

probability for triggering these events. We assume that the total mutation probability ϖ is (statistical) the same in each mutation process.

When, therefore, the probability to find the elitist component in the monotonous sequence is *large* then nature only needs a *small* tunnel – probability to trigger the mutation (as with a dice game in which the desired combination (W_s) often occurs, the player needs fewer dice rolls (P), than in a dice game in which the desired combination rarely occurs).

Therefore, it is

$$\frac{P_2}{P_1} = \frac{W_{s1}}{W_{s1+1}} \qquad (28)$$

and from eq.(16) and from eq. (26) follows

$$\exp\left\{+\frac{1}{k_B}\left[k'\left(t_{01}-t_{02}\right)+\frac{\Delta E_2}{t_{02}}-\frac{\Delta E_1}{t_{01}}\frac{t_{02}-t_{01}}{t_{02}}-\Delta_S\right]\right\}=\frac{P_2}{P_1}=\frac{1}{\sigma}\cdot\frac{s+1}{s_1+1} \qquad (29)$$

$$\left[\frac{\Delta E_2}{t_{02}}-\frac{t_{02}-t_{01}}{t_{02}}\cdot\frac{\Delta E_1}{t_{01}}-\Delta_s+k'\left(t_{01}-t_{02}\right)\right]-k_B\ln\left[\frac{1}{\sigma}\cdot\frac{s+1}{s_1+1}\right]=0 \qquad (30)$$

Equation (30) describes the change of temperature and energy necessary to provoke the lengthening of a monotonous sequence for one position to s_1+1.

The first mutation event which generates the length s_1 can be a hydrogen bond with the characteristic temperature t_{01}, and the second mutation event which generates the length s_1+1 can be a hydrogen bond with the characteristic temperature t_{02}. However, in the lengthening of a monotonous sequence the same base type is always attached to the end. Therefore, the characteristic temperature remains the same at each lengthening of one and the same monotonous sequence.

Therefore it is easier to calculate only these types of changes which always relate to the same monotonous sequences.

If so $t_{01}=t_{02}=t_0$, therefore, when the consecutive tunnel proceedings take place either at a G/C - or an A/T – hydrogen bond then

$$\Delta_C-\Delta_S=k_B\ln\left[\frac{1}{\sigma}\cdot\frac{s+1}{s_1+1}\right] \qquad (31)$$

In the equation's left side there is an entropy change

$$\Delta_C=\frac{E_2}{t_0}-\frac{E_1}{t_0} \qquad (14)$$

which relates to the characteristic temperature t_0, and an entropy change

$$\Delta_S=\frac{E_2}{t_2}-\frac{E_1}{t_1} \qquad (9)$$

E_1 and E_2 are the energies relating to the temperatures in each case provoking the tunnel process 1 or 2, respectively.
s_1 is the previous length of the monotonous sequence, which has been lengthened by one position. s is the total number of substituting bases. Equation (31) can be written as

$$\left[\Delta_S - \Delta_C\right] + k_B \ln\left[\frac{1}{\sigma} \cdot \frac{s+1}{s_1+1} = 0\right] \qquad (32)$$

If there are two tunnel proceedings, where $E_1 = E_2 = E$ then

$$\Delta_S + k_B \ln\left[\frac{1}{\sigma} \cdot \frac{s+1}{s_1+1}\right] = 0 \qquad (32a)$$

6. Interpretation of the equation (32)

From the equation (32) one finds that the left bracket represents the entropy change between two mutations whereas the right bracket is a measurement of the DNA – distribution order. The equation (32) shows that the smaller the new environmental temperature t_2 in comparison with t_1, the larger becomes the distribution order (by enlarging of the monotonous sequence length s_1). The influence of the energies E_1 and E_2 is determinate by the base rivalry.
If occurs a temperature decrease from t_1 to t_2, then any time occurs an irreparable mutation of an s_1-digit up to an (s_1+1)-digit monotonous sequence. One must take into account that this can occur only in tunnel effects (caused by base-rivalry) within long spaces of time or in a large number of DNA – fragments since the tunnel process is rare.
In section 5 we have stated a hypothesis concerning the relation between the physical and the statistical probability in case of base rivalry. From this hypothesis the equation (32) is derived.
It must be noted that the equation (32) has nothing to do with the Boltzmann equation of statistical thermodynamics. The reason is that the Boltzmann equation explains the entropy in a statistical view which expresses the coherence between entropy and probability. By way of contrast, the equation (32) is the outcome of the hypothetical equation (28).The equation (32) says that (in case of base rivalry) tunnel probability and distribution probability are so connected as expressed in this equation. Only for the phenomenona “tunnelling” and “base rivalry” the equation (32) was formed.
To prove the equation (32), we have to investigate therefore, how the base rivalry as well as the tunnel probability depend on temperature, and to what extent the DNA – distribution order is relevant to the base rivalry energy. Let us look at two succeeding mutation events which are provoked by base rivalry [where the tunnel probability depends on temperature concerning equation (4)]:
At a monotonous sequence replication, the energy needed for an irreparable hydrogen bond creation *and* the energy needed for a tunnel process are only then reached if the monotonous

sequence is long enough to accelerate the competing base components to a high energy level. The necessary length of the monotonous sequence depends on the viscosity of the braking nucleoplasm. The viscosity depends on the temperature, which is small at high temperatures; thereby, the competing base components obtain high energy after only a few replication steps. The viscosity becomes larger at low temperatures; thereby the required number of replication steps needed to provoke an irreparable lengthening of the monotonous sequence increases.

Therefore, the original length s_1, where the monotonous sequence lengthening begins, depends on temperature. At higher temperatures, s_1 is small; at lower temperatures, s_1 is large. This corresponds with the equation (32): The left bracket enlarges if t_2 becomes smaller (temperature decrease from process 1 to process 2); so the right bracket must become smaller, and this is only possible by the enlarging of the monotonous sequence length s_1. A numerical example for two proceedings shows that the equation (32) comes true with the supposed values of viscosity, fragment length, original temperature t_1, and end – temperature t_2.

The object which is to be examined is a residual fragment (fig.5) which lived in a former period (surrounding temperature t_1=313K, cytoplasm viscosity $\eta_1 = 2.285 \cdot 10^{-3}\, Pa \cdot s$)

GGGGGAACGAATACA

→ Replication direction

Fig.5: Original residual fragment

The large base rivalry energy (developed through replication of the monotonous sequence GGGGG) is calculated by the equation

$$T_k = k\left(\frac{e_0^2}{r_1} - \frac{e_0^2}{r_B}\right) - z \cdot \sqrt{\frac{e_0^2}{r_1} - \frac{e_0^2}{r_B}} \qquad (1)$$

[1]. With k_1=5 and $\eta_1 = 2.285 \cdot 10^{-3}\, Pa \cdot s\, (corresp.to\, z_1 = 6.9055 \cdot 10^{-6}\, cm\, g^{\frac{1}{2}} s^{-1})$ we receive

T_5=14.196 eV

This base rivalry energy works on the next position 6. Considering the ground state energy -13.656 eV the donor of a competing base component dGTP receives energy

E_6=-13.656+14.196=0.54 eV

and so reaching the tunnel energy area. Besides the donor of the competing base component receives energy above the quantum mechanical energy level n=2 (-3.414eV) so that the binding energy of new hydrogen bond G-C enlarges so much that the

repair mechanism cannot work. So we have the irreparably mutated residual fragment fig 6:

GGGGGGACGAATACA

→ Replication direction

Fig.6: Mutated residual fragment

We expect that this procedure really took place in the former period.

In a later period (surrounding temperature t_2=312.5K, $\eta_2 = 3.254 \cdot 10^{-3}\, Pa \cdot s$ a second irreparable mutation caused by base rivalry takes place. The second base rivalry energy (developed through replication of the monotonous sequence GGGGGG) is calculated as

T_6=14.196 eV

with the same formula as above and k_2=6 and

$$\eta_2 = 3.254 \cdot 10^{-3}\, Pa \cdot s\, (corresp.to\, z_2 = 9.85 \cdot 10^{-6}\, cm\, g^{\frac{1}{2}} s^{-1})$$

This base rivalry energy works on the next position 7. So the same procedure is held not at position 5 but at position 6. We expect that this procedure takes place and the donor of a competing base component receives also here the energy

E_7=-13.656+14.196=0.54 eV

Note that E_7=E_6=E=0.54 eV.

Finally, from fig.5 and from fig.6 we get (**s**ubstituting base G)

$$\frac{1}{\sigma} \cdot \frac{s+1}{s_1+1} = \frac{5}{6} \cdot \frac{6+1}{5+1} = \frac{5 \cdot 7}{6 \cdot 6}$$

$$s_1 = 5$$

$$\sigma_1 = 5$$

$$\sigma_2 = 6$$

$$\sigma = \frac{\sigma_2}{\sigma_1} = \frac{6}{5}$$

Inserting these parameters and t_1 = 313K and t_2 = 312.5K into equation (32a):

$$0.54\left(\frac{1}{312.5} - \frac{1}{313}\right) + 0.863 \cdot 10^{-4} \ln\left(\frac{5 \cdot 7}{6 \cdot 6}\right) = 5.19 \cdot 10^{-6} \approx 0$$

shows a good agreement. Consequently, assume that the equation (32) is correct.

7. Evolution physics

It seems to be justified, these calculations to transfer to the theory of evolution. In the history of the earth are happened many temperature changes. Warm and cold periods alternated. Especially the transition from a warm to a cold period has created higher forms of species. Normally, we explain this phenomenon with the help of theory of Darwinism.

With the help of equation (32) we also receive another explanation: When after a warm period follows a cold period then (in a large DNA – lot) will occur irreparable mutations because of base rivalry. These mutations will always lead to an increase of the order of distribution of DNA. So it is conceivable that in early warm periods only plain forms of DNA have existed with very short (monotonous) sequences (with a length 3).These short (monotonous) sequences must have lengthened themselves through temperature decrease considering of equation (32) because the cytoplasm viscosity has enlarged itself. Thus, with change from warmer down to always colder periods (caused by slowly cooling of earth) the order of distribution of DNAs has increased itself slowly, so that always more longer monotonous sequences have developed themselves. It is very remarkable that already small temperature changes (within a long period) are a cause of irreparable mutations, as one sees in the calculated example in section 6.

So we can realize that the order of DNA – distribution increases itself in the long term by long persistent temperature decrease correspondingly to the equation (32) and therefore, each period forms its own species independently of evolution - stress, only by the equation (32).

8. Mutation physics

A similar effect of the equation (32) is when viruses will be brought in a large amount from a warm area into a cold area for a certain period. Look at an animal body in which each cell is infected by the same virus. The virus replication happens synchronously with the host replication. The residual fragment of the virus is a replication unit. We assume that each 100^{th} residual fragment of the virus is a sequence as shown in fig.6.

If the animal – body possesses 10^{12} cells, then 10^{10} virus – residual fragments are alike. These fragments are replicated in each 36000^{th} second. Considering eq. (27) we expect an irreparable mutation of the second example in section 6 with the total probability

$$\varpi = P \cdot W_6$$

in each of the 10^{10} virus-residual fragments every 36000 seconds. Let be $P = 36 \times 10^{-12}$. Using the figure 6 (for determination of parameters of formula 21)

we get W_6 = 0.857. Then will be expected

$$36 \times 10^{-12} \times 0.857$$

mutations in each of the 10^{10} virus–residual fragments every 36000 seconds:

$$\frac{36 \cdot 10^{-12} \cdot 0.857}{36000\,s} = \frac{857\ irrep.vir.mut.}{10^{18}\ s}$$

in each of the 10^{10} virus–residual fragments. Therefore, in the entire animal–body will occur

$$\frac{857 \cdot 10^{10}\ irrep.vir.mut.}{10^{18}\ s} = \frac{857 \cdot 10^{10}\ irrep.vir.mut}{10^{10} \cdot 27777.8\,hours} = \frac{1\ irr.vir.mut}{32.4\ hours}$$

This means that one irreparable virus mutation in the animal is expected after every 32.4 hours.

With a view of the equation (32a) by using the same parameters as in section 6 one sees that the equation comes true if the warm area has the temperature t_1 =313K and the cold area t_2 = 312.5K. The equation (32) becomes also true with t_1 =310K and t_2 = 309.5K.

In a refrigerator or in a cold-storage house, gradual reduction of temperature goes very much faster than in normal surroundings, and the production of antibodies is reduced. So the irreparably mutated viruses will not be suppressed.

When so animals which are infected by a virus in a warm area, after that are exposed to very low temperatures then this can be the cause for suddenly occurring dangerous virus mutations in birds or in other animals, and where the transmission to human beings cannot be excluded.A lengthening (caused by base rivalry) of a monotonous sequence can only happen, when the viscosity of the nucleoplasm increases itself. Increased viscosity causes a longer path of the competing base components until they have reached the necessary energy. A larger nucleoplasm viscosity is only possible in a long period of temperature decrease or by a cold influence on a large virus fragment number (as in the calculated example: Viruses of a host remain in a warm area within a long period, and then in a cold area within a long period).

In case of base rivalry, an increase of DNA-distribution order is only possible by temperature decrease. The same is represented by the equation (32).

9. Summary

In small DNA-fragments, in the case of monotonous sequence replication there are two processes which can occur:

1. The change of thermodynamic entropy
2. The change of DNA-distribution

In this treatise, the attempt was made to find a connection between both processes: At an irreparable mutation (caused by base rivalry) there is a mathematical connection between the

temperature change and the change of the order of DNA distribution: Within a long time period or in a large number of DNA-fragments there exists the equation

$$\left[\Delta_S - \Delta_C\right] + k_B \ln\left[\frac{1}{\sigma} \cdot \frac{s+1}{s_1+1} = 0\right],$$

where the left bracket is the change of thermodynamic entropy, and the right bracket is a measurement of DNA-distribution order (monotonous sequence length s_1 enlarged up to s_1+1). This equation could be useful for the theory of evolution and besides for clearing up of virus mutations.

References

[1] W. D. Drechsel, Tumour physics. Mathematical Biosciences 213 (2008) 135-140

[2] P. Ö. Löwdin, Quantum genetics and the aperiodic solid. Some aspects on the biological problems of heredity, mutations, aging, and tumors in view of the quantum theory of the DNA molecule. Uppsala, Sweden, Uppsala Univ., Quantum Chemistry Group for Research in Atomic, Molecular and Solid-state Theory, 1963

[3] W. D. Drechsel, Berechnungen der Tunnel – Wahrscheinlichkeit in biologischen Wasserstoffbrückenbindungen Available at: http://www.basenkon.com/also-tunnel-8.pdf

[4] Jan Florian and Jerzy Leszczynski, Spontaneous DNA Mutations Induced by Proton Transfer in the Guanine-Cytosine Base Pairs: An Energetic Perspective. J. Am. Chem. (1996) 3010-3017

[5] Yongho Kim, Sangbae Lim, Yangsoo Kim, The Role of a Short and Strong Hydrogen Bond on the Double Proton Transfer in the Formamidines Formic Acid Complex: Theoretical Studies in the gas phase and in solution. J. Phys. Chem A (1999) 6632-6637.

[6] Henryk Chojnacki, Jozef Lipinski, and W. Andrzej Sokalski, Potential Energy Curves in Complementary Base Pairs and in Model Hydrogen Bonded Systems. International Journal of Quant Chemistry, Vol XIX (1989) 339-346

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