Quantum spin model fitting the Yule distribution of oligonucleotides in DNA

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Abstract

A quantum spin chain is identified by the the labels of a vector state of an irreducible representation of \( U_q(\mathfrak{sl}_2) \). The intensity of the one-spin flip is assumed to depend from the variation of the labels. The rank ordered plot of the numerically computed, averaged in time, transition probabilities is nicely fitted by a Yule distribution, which is the observed distribution of the ranked short oligonucleotides frequency in DNA

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1 Introduction

Quantum spin chains are extremely important tools to understand various physical situations and, in some cases, provide completely soluble models. An interesting field of applications of these models is the theory of molecular biological evolution. Since 1986, when Leuthäusser [1] put a correspondence between the Eigen model of evolution [2] and a two-dimensional Ising model, many articles have been written representing biological systems as spin models. Recently in [3] it has been shown that the parallel mutation-selection model can be put in correspondence with the hamiltonian of an Ising quantum chain and in [4] the Eigen model has been mapped into the hamiltonian of one-dimensional quantum spin chains. In this approach the genetic sequence is specified by a sequence of spin values $\pm 1$. DNA is build up a sequence of a four basis or nucleotides which are usually identified by their letter: C, G, T, A (T being replaced by U in RNA), C and U (G and A) belonging to the purine family, denoted by R (respectively to the pyrimidine family, denoted by Y). Therefore in the case of genome sequences each point in the sequence should be identified by an element of a four letter alphabet. As a simplification one identifies each element according to the purine or pyrimidine nature, reducing to a binary value, see [5] for a four-state quantum chain approach. The main aim of the works using this approach, see [6, 7, 8], is to find, in different landscapes, the mean ”fitness” and the ”biological surplus”, in the framework of biological population evolution. As standard assumption, the strength of the mutation is assumed to depend from the Hamming distance between two sequences, i.e. the number of sites with different labels. Moreover usually it is assumed that the mutation matrix elements are vanishing for Hamming distances larger than 1, i.e. for more than one nucleotide changes. The Hamming distance assumption is clearly unrealistic in the domain of genetic mutations. On the other side Martindale and Konopka [9] have remarked that the ranked short (ranging from 3 to 10 nucleotides) oligonucleotide frequencies, in both coding and non-coding region of DNA, follow a Yule distribution. We recall that a Yule distribution is given by $f = a n^k b^n$, where $n$ is the rank and $a$, $k < 0$ and $b$ are 3 real parameters. In this paper we propose a quantum spin model in which the intensity of the transition matrix depends in some way from the whole distribution of the nucleotides in the sequence. At present we assume that the transition matrix does not vanish only for total spin flip equal $\pm 1$, induced by the action of a single step operator, which generally is equivalent
to one nucleotide change. The model, which can appear unphysical if applied to a quantum spin chain, should be considered on the light of the previous remarks on the application to the biological evolution and our aim is to look for solutions which can reproduce the observed oligonucleotides distribution.

2 Mutations and Crystal basis

A sequence of N ordered nucleotides, characterized only by the purine or pyrimidine character, can be represented as a vector belonging to the N-fold tensor product of the fundamental irreducible representation (irrep.) (labelled by $J = 1/2$) of $U_{q \to 0}(sl_2)$ \[10\], which is usually called crystal basis representation. This parametrization allows to represent, in a simple way, the mutation of a sequence as a transition between states, which can be subjected to selection rules and whose strength depends from the two concerned states. So we identify a N-nucleotidic sequence as a state

$$| J \rangle = | J_3, J^N, \ldots, J^i, \ldots, J^2 \rangle$$

where $J^N$ labels the irrep. which the state belongs to, $J_3$ is the value of the 3rd diagonal generator of $U_{q \to 0}(sl_2)$ ($2J_3 = n_R - n_Y$, $n_x$ being the number of $x$ elements in the sequence) and $J^i$ ($2 \leq i \leq N - 1$) are $N - 2$ labels needed to remove the degeneracy of the irreps. in the tensor product in order to completely identify the state and which can be seen as identifying the irrep. which the sequence truncated to the $i$-th element belongs to. We introduce a scalar product, such that

$$\langle J | K \rangle = \begin{cases} 1 & \text{if } J_3 = K_3 \text{ and } J^i = K^i \forall i \\ 0 & \text{otherwise} \end{cases}$$

As an example, we can consider a trinucleotidic string ($N = 3$) and label the eight different spin chains in the following way($| J_3, J^3, J^2 \rangle$, $R \equiv \frac{1}{2} \equiv \uparrow$, $Y \equiv -\frac{1}{2} \equiv \downarrow$):

$$\uparrow\uparrow\uparrow = | \frac{1}{2}, \frac{1}{2}, 0 \rangle \quad \uparrow\uparrow\uparrow = | \frac{1}{2}, \frac{1}{2}, 0 \rangle$$
$$\uparrow\downarrow\downarrow = | -\frac{1}{2}, \frac{1}{2}, 1 \rangle \quad \uparrow\downarrow\downarrow = | \frac{1}{2}, \frac{1}{2}, 1 \rangle$$
$$\downarrow\downarrow\downarrow = | -\frac{3}{2}, \frac{3}{2}, 1 \rangle \quad \downarrow\downarrow\uparrow = | -\frac{1}{2}, \frac{3}{2}, 1 \rangle$$
$$\downarrow\uparrow\uparrow = | \frac{1}{2}, \frac{3}{2}, 1 \rangle \quad \uparrow\uparrow\uparrow = | \frac{3}{2}, \frac{3}{2}, 1 \rangle.$$
Flipping the total spin by ±1 ($\Delta J_3 = \pm 1$) can induce a transition to a state belonging or not belonging to the irrep. of the original state. One can easily realize that to identify a nucleotidic sequence as a state of an irrep. requires to fix the number of RY “contracted couples” occurring in the considered sequence (contraction should be understood in the same sense of contraction of creation-annihilation operators in the Wick expansion). Therefore flipping a spin implies or the creation or the deletion of a RY contracted couple, corresponding respectively to a variation of -1 or +1 of the value of the $J^N$ and, possibly, of some others $J^i$ ($2 \leq i \leq N - 1$), or to leave unmodified the number of contracted couples (so that $\Delta J^N = 0$, but $\Delta J^i \neq 0$ for some values of i). Note that alternatively one can identify $1/2 \equiv (C,G)$ and $-1/2 \equiv (T,A)$. Below we give phenomenological arguments for our choice.

3 Transition operators

Let us consider a N-nucleotidic string and classify the different transitions on the string labels $J_3, J^N, \ldots, J^2$. We can distinguish different string configurations around the $i$-th position, so that a single nucleotide mutation in $i$-th position can correspond to different variations in the string labels. We call left (right) side free the nucleotides on the left (right) of $i$-th position and not contracted with another one on the same side. Let $R_l$ be the initial (before mutation) number of the left side free purines and $Y_r$ the initial number of the right side free pyrimidines. We want to count the total number of contracted RY couples (before and after mutation) in the string, so we call $R_{in}$ ($R_{fi}$) the number, in the initial (final) state, of R preceding some Y and not contracted with any Y on their side. In the same way, with $Y_{in}$ ($Y_{fi}$) we refer to the number of Y following some R and not contracted with any R on their side. If a $R \rightarrow Y$ mutation ($\Delta J_3 = -1$) occurs in $i$-th position, then $R_{in} = R_{fi} + 1$ and $Y_{in} = Y_{fi} - 1$, where $R_{in} = R_l + 1$ and $Y_{in} = Y_r$. Now we can write the transition part of the hamiltonian, for the different possible initial configuration of the string. The transitions inducing operators are built by means of $J_-, A_i, A_{i,k}$ and their adjoint operators, as below defined.

- If $R_i = Y_r$ we distinguish two subcases:
1. $R_l = Y_r \neq 0$

$$H_1 = \sum_{i=2}^{N-1} \sum_{k=i+1}^{N} \alpha_{ik}^1 (A_{i,k}J_- + J_+ A_{i,k}^\dagger)$$ (3)

2. $R_l = Y_r = 0$

$$H_2 = \alpha_2 (J_- + J_+)$$ (4)

- If $R_l > Y_r$ we distinguish two subcases:
  1. $Y_r = 0$

$$H_3 = \sum_{i=2}^{N} \alpha_3^i (A_i J_- + J_+ A_i^\dagger)$$ (5)

  2. $Y_r \neq 0$

$$H_4 = \sum_{i=3}^{N-1} \alpha_4^i (A_i J_- + J_+ A_i^\dagger)$$ (6)

- If $R_l < Y_r$ we distinguish two subcases:
  1. $R_l = 0$

$$H_5 = \sum_{m=2}^{N} \alpha_5^m (J_- A_m^\dagger + A_m J_+)$$ (7)

  2. $R_l \neq 0$

$$H_6 = \sum_{i=2}^{N-2} \sum_{k=i+1}^{N-1} \alpha_{ik}^6 (A_{i,k} J_- A_{k+1}^\dagger + A_{i,k}^\dagger A_{k+1} J_+)$$ (8)

where $J_+$ and $J_-$ are the step operators defined by Kashiwara [10], acting on an irreducible representation with highest weight $J^N$, i.e. inducing the transitions $\Delta J_i = 0, \forall i \neq N$,

$$A_{i,k} \mid J \rangle = \mid J_3, J^N, \ldots, J^k, J^{k-1} - 1, \ldots, J^i - 1, J^{i-1}, \ldots, J^2 \rangle$$

$$\quad (2 \leq i \leq N - 1 \quad i + 1 \leq k \leq N)$$ (9)

$$A_i \mid J \rangle = \mid J_3, J^N - 1, \ldots, J^i - 1, J^{i-1}, \ldots, J^2 \rangle$$

$$\quad (2 \leq i \leq N)$$ (10)
Therefore $A^\dagger_{i,k}$ is the operator which increase by 1 the value of $J^l$, for $k-1 \leq l \leq i$. A few words to comment on the above equations. Let us consider a mutation $R \to Y$ which involve a transition $\Delta J_N = -1$ (case $R_l > Y_r$); as of the considered transition also entails $\Delta J_3 = -1$, we have to apply the operator $J_-$, as well as the operator $A_i$. Of course, first we have to lower by 1 the value of $J_3$, then to modify $J^N$, otherwise the initial state may eventually be annihilated, even if the transition is allowed (in the case $J^N - 1 < J_3$). Likewise, in correspondence of a transition $Y \to R$ ($\Delta J_3 = +1$), first the change $J^N \to J^N + 1$ has to be made, then $J_3 \to J_3 + 1$. If we want to write a self-adjoint operator, we have to sum the operator which gives rise to the transition $Y \to R$ with that one which leads to $R \to Y$, leaving the rest of the string unmodified, so

$$A_i J_- + J_+ A^\dagger_i.$$  \hfill (11)

This operator leads to the mutation $Y \to R$ or $R \to Y$ for a nucleotide in $i$-th position, in a string with $R_l > Y_r$. If the mutation $R \to Y$ corresponds to a rising of $J^N$ (i.e. a transition with $\Delta J_N = 1, \Delta J_3 = -1$, case $R_l < Y_r$), first $J^N$ has to be modified, then $J_3$; therefore we write the self adjoint operator

$$J_- A^\dagger_m + A_m J_+$$  \hfill (12)

The above operator gives rise to mutations $R \to Y$ and $Y \to R$ for a nucleotide in $i$-th position, preceding the $m$-th one, in the case $R_l = 0, Y_r \neq 0$.

Let us remark that eq. (11) is included in eq. (5), if the coupling constants $\alpha$ are assumed equal; in eq. (8), only the writing order for $A_{k+1}$ (and its adjoint) and $J_\pm$ has to be respected. Assuming now that the coupling constants do not depend on $i, k, m$, we can write that transition hamiltonian $H_I$ as

$$H_I = \mu_1 (H_3 + H_5) + \mu_2 H_1 + \mu_3 H_2 + \mu_4 H_6$$  \hfill (13)

We let the fenomenology suggests us the scale of the values of the coupling constants of $H_I$. We want to write an interaction term which makes the mutation in alternating purinic/pyrimidinic tracts less likely than polipurinic or polipyrimidinic ones. We mean as a single nucleotide mutation in a polipurinic (polipyrimidinic) tract, a mutation inside a string with all nucleotides $R$ ($Y$), i.e. a highest (lowest) weight state. Such a transition corresponds to the selection rules $\Delta J_N = -1, \Delta J_3 = \pm 1$, i.e. a transition generated by the action of $H_3$ and $H_5$. In the iteration term $H_I$, we give them a coupling constant smaller than the others terms. We introduce, for...
\[ \Delta J_3 = \pm 1 \], only four different mutation parameters \( \mu_i \) \((i = 1, 2, 3, 4)\), with \( \mu_1 < \mu_k k > 1 \).

1. \( \mu_1 \) for mutations which change the irrep., \( \Delta J^N = \pm 1 \), and include the spin flip inside an highest or lowest weight vector;

2. \( \mu_2 \) for mutations which do not change the irrep., \( \Delta J^N = 0 \), but modifies other values of \( J^k \), \( \Delta J^k = \pm 1 \) \((2 \leq k \leq N - 1)\);

3. \( \mu_3 \) for mutations which do not change the irrep., \( \Delta J^N = 0 \), neither the other values of \( J^k \), \( \Delta J^k = 0 \), \((2 \leq k \leq N - 1)\);

4. \( \mu_4 \) for mutations which change the irrep., \( \Delta J = \pm 1 \), but only in a string with \( 0 \neq R_l < Y_r \).

We do not introduce another parameter, for mutations generated by \( H_4 \), i.e. \( i \)-th nucleotide mutation in a string with \( R_l > Y_r \neq 0 \), to not distinguish, in a polipurinic string, between a mutation in 2-th position and another one inside the string.

Let us emphasize once more that the proposed model takes into account, at least partially, the effects on the transition in the \( i \)-th site of the distribution of all the spins.

### 4 Results

The total hamiltonian of the model will be written as \( H = H_0 + H_I \), where \( H_0 \) is the diagonal part in the choosen basis and, in the following, is assumed to be \( H_0 = \mu_0 J_3 \). In order to evaluate the probabilities of transition, we cannot analytically study the time evolution of an initial state, representing a given spin chain, as ruled by hamiltonian \( H \). So we look for a numerical solution, with a suitable choice of the value of the parameters, for \( N = 3, 4, 6 \). Before solving numerically the model, it may be useful to point out explicitly its main features. \( H_0 \) is the hamiltonian of a spin chain in presence of an uniform, constant, magnetic field (in the biological system it is the "fitness" assumed proportional to total purine surplus). \( H_I \) describes an interaction on the \( i \)-th spin neither depending on the position nor on the nature of the closest neighbours. Indeed it depends on the "ordered" spin orientation surplus on the left and on the right of the \( i \)-th position. Should it not depend on the order, it may be considered as a mean-field like effect.
Moreover $\Delta J_3 = \pm 1$ transitions are allowed, which can be considered or as the flip of a spin combined with an exchange of the two, oppositely oriented, previous or following spins or as the collective flip of particular three spin systems, containing a two spin system with opposite spin orientations (see example below). Biologically, the transition depends in some way on the ”ordered” purine surplus on the left and on the right of the mutant position. For example, the matrix form of $H$, on the above basis (for $N = 3$) is the following one, up to a multiplicative dimensional factor $\mu_0$

$$ H = \begin{pmatrix} -1 & \delta & 0 & \gamma & \epsilon & 0 & \epsilon & 0 \\ \delta & 1 & 0 & 0 & 0 & \epsilon & 0 & \epsilon \\ 0 & 0 & -1 & \delta & \epsilon & 0 & \epsilon & 0 \\ \gamma & 0 & \delta & 1 & 0 & \epsilon & 0 & \epsilon \\ \epsilon & 0 & \epsilon & 0 & -3 & \delta & 0 & 0 \\ 0 & \epsilon & 0 & \epsilon & \delta & -1 & \delta & 0 \\ \epsilon & 0 & \epsilon & 0 & 0 & \delta & 1 & \delta \\ 0 & \epsilon & 0 & \epsilon & 0 & \delta & 3 & \end{pmatrix} $$

(14)

Note that the above hamiltonian depends only on three coupling constants due to the very short length of the chain. For $N \geq 4$ the 4th coupling constant (denoted in the following by $\eta$) will appear. Let us emphasize that the hamiltonian (14) does not only connect states at unitary Hamming distance. As an example, we look at the transitions allowed from $|\frac{1}{2}, \frac{1}{2}, 0\rangle$ ($\uparrow\downarrow\uparrow$) and from $|\frac{1}{2}, \frac{1}{2}, 0\rangle$ ($\uparrow\downarrow\uparrow$)

\[ \uparrow\downarrow\uparrow \rightarrow \{ \uparrow\uparrow\uparrow, \downarrow\uparrow\uparrow, \uparrow\down\uparrow \} \quad \uparrow\downarrow\downarrow \rightarrow \{ \down\uparrow\uparrow, \up\up\up, \down\up\up \} \]

The transition probability between two states shows the typical quantum-mechanical rapidly oscillating behaviour in time. We define a time-averaged transition probability ($i \rightarrow f$)

$$ < p_{if} > = \frac{1}{T} \int_0^T p_{if}(t) \, dt \quad (15) $$

where the value of $T$ will be numerically fixed to a value, such that the r.h.s. of eq.(15) is stable. For lack of space, we do not explicitly write the hamiltonian which only induces transitions between chains at Hamming distance
equal to one, with coupling constant $\beta$. Notice however that such a (Hamming) Hamiltonian is not obtained by eq. (14) putting $\delta = \gamma = \epsilon = \beta$. If we order (in a decreasing way) the average transition probability from an initial state to every other state, we obtain, using the Hamiltonian with Hamming distance, a rank-ordered distribution of transition probability like that in fig. [1] for $N = 4$. Its shape does not depend by the choice of initial state or by the coupling constant $\beta$ value. We always get the same structure, for models with transition probability only depending on Hamming distances. So the rank-ordered distribution of the average transition probability shows a plateaux structure: every plateaux contains spin sequences at the same Hamming distance from the initial one. In the case of the model which we propose here, i.e. the Hamiltonian in (14), the distribution of rank ordered average transition probability does not show a plateaux structure, but its shape is well fitted by a Yule distribution (fig. 2), like the rank ordered distribution of oligonucleotidic frequency in the strings of nucleic acids [9].

Let us observe that we obtain a Yule distribution (and not a plateaux structure) even if all parameters in (14) are tuned at the same value, which means that the distribution is the outcome of the model and not of the choice of the values of the coupling constants. Analogous results are gained for $N = 4$ (fig. 3) and $N = 6$ (fig. 4), the state labelled by 1 being the initial one.

As final remarks we point out that:

i) our model is not equivalent to a model where the intensity depends on the site undergoing the transition, or from the nature of the closest neighbours or the number of the $R$ and $Y$ labels of the sequence; indeed essentially the intensity depends on distribution in the sequence of the $R$ and $Y$;

ii) the ranked distribution of the probabilities, not averaged in time, computed for several values of the time follows generally a Yule distribution law; for the highest value of $N$, the distribution is equally well fitted by a Zipf law, but not for the lowest values of $N$, in agreement with the remark of [9].

In conclusion we are far from claiming that our simple quantum mechanical model explains the observed oligonucleotide distribution for several obvious reasons. Apart from the extremely simplifying assumption made (initial state as a pure state) and from the fact that we are really comparing different data, the experimental ones being derived from the splitting in short oligonucleotide sequences of several far longer sequences, we are relating quantities computed in a quantum world to classical observables. In any way we believe that the proposed model exhibits intriguing and interesting features, hinting
in the right direction, which are worthwhile to be further investigated, in particular either to make more clear the connection quantum model-classical quantities either to reformulate our transition matrix in order to be inserted in a classical master equation. It is worthwhile to remark that we are trying to compare theoretical results, deriving from a simple model (depending only on 4 parameters for any N), to really observed data, coming from the extremely complex biological world. More details and further developments will be presented in a longer paper.

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Figure 1: Rank ordered distribution of time-averaged transition probability from the initial status ↑↑↓ for a dynamics generated by Hamming hamiltonian, with $\beta = 0.5$. The first point is out of the graph.

Figure 2: Rank ordered distribution of time-averaged transition probability $f$ from the initial status ↑↑↓ for a dynamics generated by $H$ with $\epsilon = 0.1$, $\gamma = \delta = 0.3$. The distribution was fitted by a Yule function (continuous line) $f = aR^{bR}$ ($R$ is the rank). The parameters was estimated as $a = 1.96$, $b = 0.24$, $k = -1.49$. 
Figure 3: Rank ordered distribution of time averaged transition probability $f$ from the initial status $\downarrow\downarrow\uparrow\downarrow$ for a dynamics generated by $H$, with $\epsilon = 0.1$, $\gamma = \delta = \eta = 0.5$. The distribution was fitted by a Yule function (continuous line) $f = aR^k b^R$ ($R$ is the rank). The parameters were estimated as $a = 0.60$, $b = 0.72$, $k = -0.64$.

Figure 4: Rank ordered distribution of time averaged transition probability $f$ from the initial status $\uparrow\downarrow\uparrow\uparrow\uparrow$ for a dynamics generated by $H$, with $\epsilon = 0.1$, $\gamma = \delta = \eta = 0.5$. The distribution was fitted by a Yule function (continuous line) $f = aR^k b^R$ ($R$ is the rank). The parameters were estimated as $a = 0.21$, $b = 0.95$, $k = -0.66$. 

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