Amino Acids (1999) 17: 1–129

Amino
Acids
© Springer-Verlag 1999
Printed in Austria

6th International Congress on Amino Acids

Bonn, Federal Republic of Germany
August 3–7, 1999

Abstracts

Presidents:
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This congress was sponsored
by the Red Bull Company, Salzburg, Austria

1. To draw a small scale phylogenetic tree by a core set of population and expand the tree to the whole set;
2. To only use a partial region of sequences to reconstruct trees effectively after alignment.

In this paper, we introduce an efficient algorithm based on information theory to realize above two ideas. We also show the robustness and the quality of our method by using the computer simulation.

Analysis of the disease course for HIV by chaos degree

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There exist several different quantities to measure chaotic aspects of dynamical systems. A new measure has been introduced in [1], which is called the entropic chaos degree and it was successfully applied to some dynamics in physics [2]. Here we use this entropic chaos degree to analyze the variation of human immunodeficiency virus as we did in [3, 4]. That is, we calculate the entropic chaos degree of the dynamics reduced from the variation of V3 regions of HIV which are obtained from patients infected with HIV-1 at various times after seroconversion or infection. If the variations of genome have chaotic aspects, it can be considered that the state of the disease progression is characterized by the entropic chaos degree. As a result, the chaos degree for the dynamics changing V3 region shows the specific variation patterns throughout from primary infection to death after having AIDS. The variation patterns indicate that the entropic chaos degree is useful to infer patient's condition of disease progression.

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Oxidative stress and DNA-repair-deficiency, potential causes for neurodegeneration in Down syndrome?

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Oxidative stress in combination with a DNA-repair-deficiency results in severe DNA-damage. This failure has been proposed to be a trigger for the cell loss and for neurodegenerative changes like regional cortical atrophy in brain of patients with Down syndrome (DS, Trisomy 21) and Alzheimer's disease (AD). SOD, catalase, gluthatione- and thioredoxin-peroxidase are known to be important for cell defence against reactive oxygen species. Data about possible failures in the activity of these antioxidant systems in blood and brain of DS patients are controversial including the "gene dosage effect" by the SOD-activity. Some controversial data have been also obtained by measuring the products of lipid-peroxidation in the brain of these patients. DNA has been found to be damaged via fragmentation. The products of DNA oxidation, however, have not been found in the brain of DS patients and AD [1].

Thus, the molecular mechanisms of cell loss and neurodegenerative changes in the brain of DS and AD patients are still unclear. Using the "gene hunting" method we were looking for the deviations in the gene regulation in DS-fetal brain and consequently for the metabolic pathways involved in this pathology. We have found upregulated DNase I which fragments DNA, but X-ray-repair-cross-complementing gene (XRCC1) generally important for DNA repair has been found to be highly upregulated as well. Moreover, very important antiapoptotic factors (NFκB, ADF, NAIP, hsp70) have been found to be crucially downregulated in comparison to the control fetal brain. These results explain the monitored DNA-damage (fragmentation) in the brain of DS patients through the highly upregulated DNase I. DNA repair is highly activated in response to the DNA damage. Decreased activities of the important antiapoptotic factors could be a cause for increased apoptosis of neurons with subsequent neurodegeneration.

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A stochastic model for the cooperative behaviour of biological systems

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The cooperativity in biological systems involves the concerted formation or rupture of many similar weak chemical bonds. A stochastic model for these transitions is proposed. This model involves only two parameters, the mean probability p and the coupling capacity Δp, but it offers a surprising wealth of different qualitative behaviours when the two parameters are varied. This model, originally devised to describe protein folding, can be applied to more general biological systems which undergo transitions following a sigmoidal curve and it seems to improve the qualitative description of these systems with respect to the more familiar deterministic models. The advantages of this stochastic model are the following: a) its simplicity, b) the fact that it depends only on two parameters, c) the relatively short simulation time required.

The cooperative systems are characterized by a sharp transition, indicating that a large variation of the *output variable* y takes place in a very small interval of the independent *state-variable* x. Significant examples of these systems are: i) the binding of four oxygen molecules to one hemoglobin molecule; ii) the thermal transition from *gel* to *sol* phase of artificial and natural membranes; iii) the unfolding of macromolecules like DNA, proteins.

All these phenomena are empirically described by a *sigmoidal curve*:

$$y = \frac{x^{\alpha}}{1 + x^{\alpha}} \tag{1.1}$$

where α is related to the *cooperativity* of the change of y. When $\alpha = 1$, the transition is non-cooperative, while for α *large* the transition tend to become *all or none* and the total change in y takes place in a very narrow interval of x.

The mean probability p, is related to $exp(-\Delta G/RT)$, (ΔG represents the mean activation free energy for the formation of a chemical bond, T is the absolute temperature and R is the Rydberg constant) so it is controlled by macroscopic variables such as temperature, *pH*, etc.

The parameter Δp, which is related with the cooperativity of real biological transitions, measures the probability of forming a new weak bond and depends on the number of similar bonds already formed: the higher the number of bonds already formed, the greater the probability that additional bonds can be formed, and vice versa. Δp can be calculated using the fact that it is relat-

ed to the steepness α, i. e. the slope of the tangent line to the sigmoidal curve at the middle point of the transition. Experimental data concerning sigmoidal curves relative to cooperative transitions in these systems have been compared with our stochastic model showing that it provides a good approximation for them. This allowed to estimate the cooperativity parameter Δp.

A method of sequential analysis by 2D-pattern formation with coloration

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The work is motivated by the demand for efficient analysis of a very long sequential data such as a DNA sequence consisting of 4 nucleotides and a protein sequence consisting of 20 amino acids. Characteristics to be searched in such a sequential data:

1. (local periodicity) Periodicity of letters observed in a relatively short segment in the long sequential data.
2. (tandem repeat) Periodic appearance of a small block of letters (both direct repeat $\rightarrow \rightarrow \rightarrow \rightarrow$ and inverted repeat $\rightarrow \leftarrow \rightarrow \leftarrow$).
3. (long period) Local periodicity with a rather long period (more than 100).
4. (distribution of particular letters) Relative frequency of observed letters and its uneven distribution in the sequential data.
5. (randomness) Randomness of the appearance of observed letters.
6. (global structure) Beyond numeric characteristics though not yet well formulated.

These are clues for (i) distinguishing particular regions in the sequence; (ii) searching duplicated regions; (iii) searching regions which are expected to play a particular role; (iv) similarity or dissimilarity among sequential data.

In this talk we shall propose a new method (patent pending in Japan 1997; in USA and Europe 1998) for searching the above mentioned characteristics. Our method consists of two steps: rearranging the sequential data into a 2-dimensional table and assigning a particular colour to each letter. Then some characteristic properties can be visualized with certain patterns to be seen by eyes, for example, the difference of coding and non-coding regions of DNA sequences, and tandem repeat sequences with different repeat length in DNA sequences. The density of colour spectrum gives a distribution of particular letters and some hierarchy of randomness is observed.

Our method possesses flexibility from some technical aspects. In particular, the way of assignment of colours is important in order to visualize a particular pattern and should be improved. On the other hand, as a future direction the mathematical theory of "global structure" will be interesting to discuss and might give a new aspect to the analysis of sequential data appearing in various research fields.

On multiple alignment of genome sequences by quantum algorithm

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Alignment is the most important operation in comparing the amino acid sequences of biological species. The computational complexity for the alignment when dynamic programming is used is $O(L^N)$, when L is the length of the sequence and N is the number of sequences; it is tremendous when N is increased. In [1, 2] we apply the simulated annealing to the multiple alignment. Here we report a new algorithm for the multiple alignment by means of quantum algorithm [3].

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A hypothetic physical mechanism for the folding of protein structural classes

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Although the number of protein sequences is extremely large, the number of their folding patterns is quite limited. Actually, owing to the very high degenerate nature of the sequence-structure relationship, proteins are generally folded into one of only a few structural classes that are closely correlated with the amino acid composition. This suggests that the interaction among the components of amino acid composition might play a considerable role in determining the structural class of a protein. To quantitatively test such a hypothesis, three potential functions were formulated that respectively represent the 0^{th}-order, 1^{st}-order, and 2^{nd}-order approximations for the interaction among the components of the amino acid composition in a protein. It was observed that the correct rates in recognizing protein structural classes by the 2^{nd}-order potential are significantly higher than those by the 0^{th}-order and the 1^{st}-order potentials, indicating that an algorithm that can more completely incorporate the interaction contributions will yield better recognition quality, further demonstrating that the interaction among the components of amino acid composition is an important driving force in determining the structural class of a protein during the sequence folding process.

Gene structure of *S*-adenosylmethionine decarboxylase and its localization on mouse chromosome

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Gene structure of mouse *S*-adenosylmethionine decarboxylase (AdoMetDC) has been determined. The mouse genome have three AdoMetDC genes (AMD1, AMD2 and AMD3). The AMD1 gene consisted of 8 exons and 7 introns, similar to the gene of rat AdoMetDC, and it was mapped to chromosome 10. The AMD2 gene was intronless gene that was previously reported and the AMD3 gene was pseudogene. AdoMetDC encoded by the intronless AMD2 gene had two amino acid replacements (Met to Ile at codon 70 and Ala to Val at codon 139), compared with the protein encoded by the AMD1 gene, and exhibited decreased cytalytic activity and decreased processing activity when expressed in AdoMetDC-deficient *E. coli*. When Ile-70 of the protein encoded by the AMD2 was converted into Met-70, both the catalytic and processing activities recovered markedly. The strength of the promoters of AMD1 and AMD2 gene was measured using the reporter assay in various cell lines. In all cell lines, the AMD1 promoter was much stronger than the AMD2