Frustration and optimization: What magnetic materials and proteins have in common

S. Kobe

Technische Universität Dresden, Institut für Theoretische Physik,

D-01062 Dresden, Germany

A basic concept to describe order phenomena in magnetic materials by simple models is optimization. The **ISING** model is constructed by associating with the orientation of an elementary magnet (spin) of the *i*-th atom a number S_i that is either +1 ($\uparrow$) or -1 ($\downarrow$). The interaction energy between the *i*-th and the *j*-th spin is $-J_{ij}S_iS_j$. Consequently, the total energy E of the system consisting of N spins is the sum over all interacting spin pairs:

$$E = -\sum_{i<j}^{N} J_{ij} S_i S_j \quad .$$

For a given set of J_{ij} the ground state with the ground-state energy E_{gs} results from $E_{gs} = \min(E)$. It is easy to see that the result of this optimization problem is trivial for positive values J_{ij}. The ground state is ferromagnetic: All spins are aligned, i.e. either all S_i are +1 or all S_i are -1.

The optimization problem becomes more complex when antiferromagnetic interations ($J_{ij} < 0$) arise: In a triangular lattice, e.g., neighbors of a given spin are also neighbors of each other. Consequently, certain interactions are prevented from being „satisfied“ in the ground state. This situation is called frustration. The concept was introduced to explain the magnetic behavior of spin glasses, a new class of magnetically ordered materials. The main ingredients constituting a spin glass model are mixed signs of J_{ij} and disorder. It is shown that finding ground states is a very hard combinatorial problem and can be exactly solved only for a restricted number of spins N.

It is a task of this talk to show that the concept of frustration and optimization can be generalized. A protein, e.g., is composed of amino acids (AA). The basic chemical structure of an AA is determined by its N-C_α-C backbone and a side chain (SC), which is linked with the C_α atom. The 20 different natural AA are distinguished by different SC. A certain protein is characterized by the sequence of AA (just as a word is characterized by the sequence of letters). The AA in the protein are connected in such a way that N, C_α and C atoms of consecutive AA form a chain.

It is one of the most demanding problems in biophysics and bioinformatics to predict the spatial structure of proteins from the sequence of their AA *only*. We have introduced a dynamical lattice model (DLM) of a protein, which is constructed on the basis of the atomic distances and bonding angles in molecules. The linkage section of two consecutive AA of this model is sketched in Fig. 1. The distances are fixed in the following way: N-C_α = 1.47 Å, C_α-C = 1.53 Å, C-N' = 1.32 Å. Analogously, the angles between the connection lines of these atoms can be fixed: N-C_α-C = 110º, C_α-C-N' = 114º, C-N'-C_α' = 123º. The crucial point is that the C_α' atom of the subsequent amino acid lies in the plane formed by the atoms C_α-C-N'. So the position of the C_α' atom respective to the position of the preceding AA in the chain is determined by three angles. Because ω is fixed additionally to 180°, there are only two remaining degrees of freedom (φ, ψ).

It is known that there is a correlation between φ and ψ, which is different from one AA to another. On the basis of a mathematical analysis of experimental data for these correlations a reduction to a few relevant discrete values (φ, ψ) can be done. Assuming that the positions of a subset of AA in a DLM protein are already fixed, the subsequent AA has only q different possibilities for its spatial position. A typical value for q averaged over all twenty amino acids is q = 3.8 leading altogether to about q^N theoretically possible conformations of a DLM protein with the sequence length N.

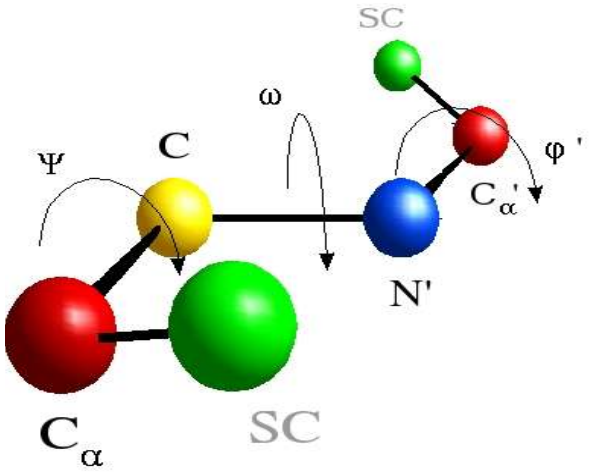

Fig. 1: Spatial representation of the linkage section of two subsequent amino acids in a protein. The atoms C_α. C, N' and C_α' lie in a plane. SC denote the side chains.

It is known that there are interactions between all AA. We assume that the interaction energy $E_{ij}(r)$ is constant between r_{min} and r_{max}, where r is the distance between the C_α atom of the AA μ at the site i and the C_α atom of the AA ν at the site j:

$$E_{ij}(r) = \begin{cases} \infty & r < r_{min} \\ e_{\mu\nu} \quad \text{for} & r_{min} \le r \le r_{max} \\ 0 & r > r_{max} \,. \end{cases}$$

The interaction constants $e_{\mu\nu}$ between the AA μ and the AA ν are taken from an analysis of experimental results. Because $e_{\mu\nu}$ can be positive or negative, i.e. the interactions are attractive or repulsive, frustration is inherent in this problem, too.

Analogously to the spin glass problem, the spatial positions of all AA in a DLM ground state for a protein with the sequence length N can be obtained via the global minimum of the total energy

$$E_{gs} = \min\left(\sum_{i<j}^{N} E_{ij}\right) \quad .$$

The obtained spatial structures of DLM proteins can be compared with the corresponding native structures measured by X-ray and NMR methods. The last-mentioned experimentally determined three-dimensional macromolecular structure data are collected in the Protein Data Bank (PDB).

We have found a remarkable agreement of our DLM results with PDB for proteins up to about N = 40. For the protein 1L2Y, e.g., a helical structure could be reproduced. Another example is insulin consisting of two chains with 21 and 30 AA, respectively. The Alzheimer's disease amyloid A40 was investigated also with respect to the postoptimal metastable configurations.

It could be a challenging task in the future to use realistic models of proteins to study energy landscapes and dynamics. Furthermore, the possibility of protein design '*in silico'* opens a new field of research.

List of selected references:

(cf. also: http://www.physik.tu-dresden.de/itp/members/kobe/index.html)

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