On the Principle of Substance Stability and Thermodynamic Feedback in Hierarchic Systems of Bioworld

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Abstract - The creation of structural hierarchies in open natural biosystems within the framework of quasi-closed systems is investigated by the methods of hierarchic thermodynamics (thermostatics). During the evolution of natural open systems, every higher hierarchic level *j* appears as a consequence of thermodynamic self-organization (self-assembly) of the structures of the lower (*j - 1*)-th level. Such a self-assembly proceeds as a result of stabilization of the *j*-th level. This is related to the Gibbs` (Helmholtz`) specific function of formation of the structure of the *j*-th level tending to a minimum. As a result of action of the principle of substance (matter) stability, the structures of the *j*-th level are enriched with less stable structures of the (*j - 1*)-th level in the course of evolution. This provides a thermodynamic feedback between the structures of the higher *j*-th level and lower (*j -1*)-th level, thus preventing full structural stabilization of the *j*-th level and causing "thermodynamic rejuvenation" of biosystems. The latter enhances "thermodynamic" deceleration of evolution and practically unlimited maintenance of life. Examples of quantitative correlations are provided that call for further application of the substance stability principle to living and nonliving hierarchic structures.

Molecular and Supramolecular Stability of Biomass Structures

The principle of stability of chemical substances or, in general, the principle of substance stability appears to be applicable to all biological systems. The essence of the principle is as follows: when *more stable* structures of the highest hierarchic level (*j*), for example, the supramolecular structure of the membrane, are formed, nature uses *lower stable* structures at a lower hierarchic level, for example, molecular level (*j - 1*). The data presented in the table below qualitatively illustrate this principle.

For example, very "chemically" thermodynamically stable substances, such as N_2, CO_2, and H_2O have comparatively low temperatures of melting and boiling,[1] which suggests qualitatively a relatively low thermodynamic stability of their condensed phases.

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[1] It goes without saying that the knowledge of the temperatures of melting T_{m_i} and boiling T_{b_i} is not sufficient for a quantitative estimate of thermodynamic stability of the supramolecular structure for substances of different chemical composition. However, when comparing the thermodynamic stabilities of substances, T_{m_i} and T_{b_i} often correlate quantitatively with these stabilities.

Gases and water – H_2, N_2, O_2 and H_2O	
$T_{mol.decay}$ 1000 – 3000 K	High molecular stability
T_{m_i} 20 – 273 K	Low supramolecular stability

Tissues – Fats (lipids), Proteins, Sugars, Nucleic acid	
$T_{mol.decay}$ 320 – 380 K	Low molecular stability
T_{m_i} 273 – 383 K	High supramolecular stability

On the other hand, energy-intensive substances with a low molecular - "chemical" thermodynamic stability such as fats, sugars, peptides and nucleic acids, melt at comparatively high temperatures and decompose during "melting" and "boiling". Aggregated (condensed) phases of these substances are very stable.

The qualitative principle formulated by the author (Gladyshev's principle) agrees with the experimental data and calculations made using the Gibbs-Helmholtz' equation and its analog (Gladyshev. 1996, 1997, 1999a, 1999b, 2001a).

Note that the principle actually states the following. The higher the specific chemical (*ch*) component of Gibbs' function, $\Delta \overline{G}_i^{ch}$ of the *i*-th chemical compound, i.e., the less thermodynamically stable it is, the lower (more negative) the specific supramolecular component of Gibbs' function, $\Delta \overline{G}_i^{im}$ of this substance corresponding to its crystallization (solidification) or condensation from the oversaturated (supercooled) state. The construction of dependence of $\Delta \overline{G}_i^{ch}$ from $\Delta \overline{G}_i^{im}$ (or $\Delta \overline{G}_{bi}^{im}$) for homologous sequences of substances, such as alkanes, high molecular weight alcohols, high molecular weight acids, etc., (when the ratio between atoms H, C, and O, remains practically unchanged upon transition from one member of the sequence to another) is comparatively rigorous evidence in favor of this statement. This does not require knowledge of absolute values of the thermodynamic functions, since the level corresponding to approximately the same ratio of initially different atoms (from which the *i*-th compounds of the above mentioned homologous sequences or, at least, highest members of these sequences, are formed) is taken as the zero level. Some examples of these dependencies are given in Figs. 1 and 2.

Figure 3 presents specific (per unit mass) Gibbs' functions of formation (at 298 K) of $\Delta \overline{G}_i^{ch}$ as a function of the temperature of melting T_{m_i} for a sequence of *n*-alkanols $C_3 - C_{20}$. This dependence also confirms the validity of the principle of chemical substance stability (Gladyshev and Kitaeva, 1995[1]).

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[1] In this paper, erroneous values of $\Delta \overline{G}_i^{ch}$ are given of *n*-alkanols C_1 and C_3.
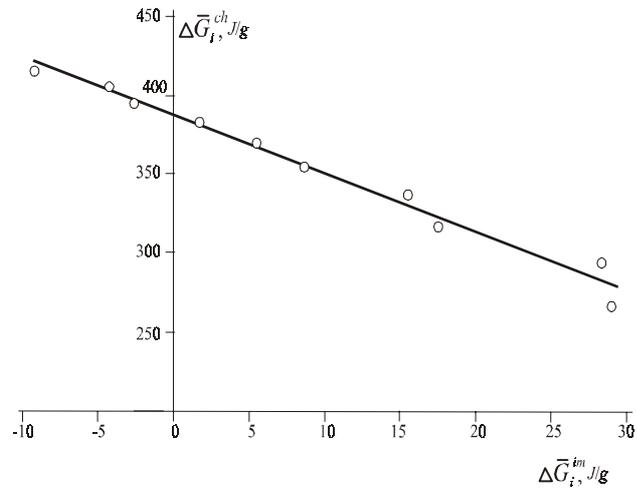
Fig. 1. Specific (per unit mass) Gibbs' function of (at 298K) of *n*-alkanes $C_{11} - C_{20}$, $\Delta \overline{G}_i^{ch}$ ($\Delta \overline{G}_f^{cho}$) as a function of specific (per unit mass) Gibbs' function of nonequilibrium phase transition during formation of supramolecular structure as a result of aggregation of these compounds (at 298K), $\Delta \overline{G}_i^{im}$. The values of $\Delta \overline{G}_i^{im}$ from $- 10$ to 0 characterize nonequilibrium transitions "supercooled liquid $\rightarrow$ solid phase". The values of $\Delta \overline{G}_i^{im} > 0$ belong to hypothetical, nonexistent, transitions "overheated liquid $\rightarrow$ solid phase". The calculation was performed using the published date (Stull et. Al., 1969; Handbook…, 1986).
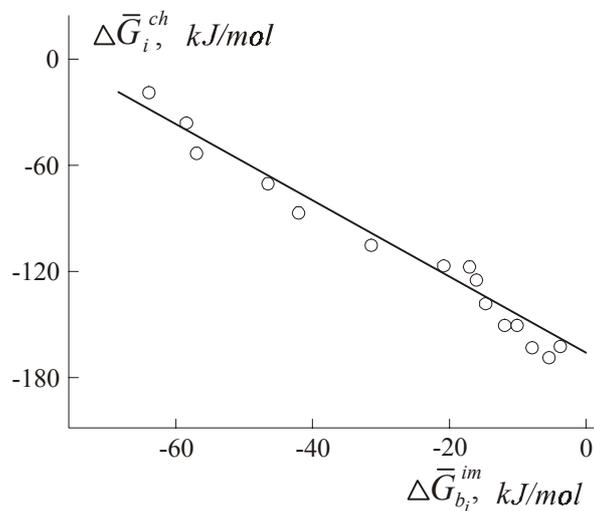

Fig. 2. Specific (per mole of substance) Gibbs' function of formation (at 298K) of *n*-alkanols C_1-C_{10}, C_{12}, C_{14}, C_{16}, C_{18}, C_{20}, $\Delta \overline{G}_i^{ch}$ ($\Delta \overline{G}_f^{cho}$) as a function of specific (per mole of substance) Gibbs' function of nonequilibrium phase transition of substances from the state of supercooled gas to the condensed state (at 298K) $\Delta \overline{G}_{b_i}^{im}$. The calculation was performed using the published data (Stull et. Al., 1969; Handbook…, 1986).

Note the following. The principle of chemical substance stability is a thermodynamic principle. It actually states that the tendency of a biosystem in evolution (ontogenesis and phylogenesis) to the appearance of comparatively highly stable structures of higher hierarchies leads to the selection of comparatively low stable structures of lower hierarchies. This evolutionary tendency of biosystems rejuvenates lower hierarchic structures, i.e., preserves the optimal stability of these structures. The existence of thermodynamic feedback or "thermodynamic rejuvenation" of living systems from the standpoint of thermodynamics delays the evolution (ontogenesis, phylogenesis) and is a cause of practically unlimited development in the bioworld. The data presented in the table confirm the principle in question.
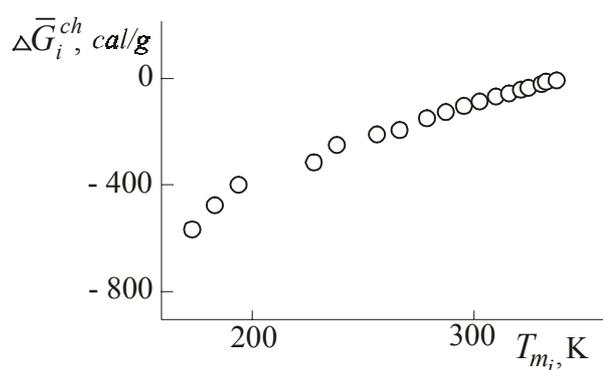

Fig. 3. Specific (per unit mass) Gibbs' function of formation (at 298 K) of $\Delta\overline{G}_i^{im}$ as a function of the temperature of melting, T_{m_i} for a sequence of n-alkanols C_3 - C_{20}. (Correlation was calculated using the data of Stull *et al.,* 1969.) The point corresponding to C_2 drops out of the general correlation and it was not plotted.

An illustrative example of the formulated principle is provided by selection of the sequence of nucleic acids including AU pairs in evolution, although these pairs are less stable from the standpoint of supramolecular thermodynamics than GC pairs.

Hence, the selection of natural (AUGC) sequences makes allowance for not only the stability of a lower molecular hierarchy, as was sometimes previously believed, but also of the stability of higher hierarchies, tertiaries, quaternaries, and the highest supramolecular structures - nucleic acid -protein complexes (Gladyshev. 1996, 1997, 2000a).

There are some facts, which call for application of the principle of substance stability to the hierarchy of cells. Thus, tumor cells have a lowered ability for aggregation. As a result, they easily move in the body, which leads to the appearance of metastases. The cell membranes of tumor cells are, apparently, formed from supramolecular structures of increased stability (Andronikashvili et al., 1983). Hence, the stability of cell aggregates formed with participation of tumor cells should be lowered according to the principle in question. In order to increase the adhesive abilities of the cells, the structure of membranes should be "diluted" and made less thermodynamically stable. Hence it is clear why experimental anticancer diets propose the use of plant fats, fats of animals from cold seas, and other products containing residues of unsaturated low-melting fatty acids. The antitumor effect of aspirin can also he explained on the basis of such statements. These ideas agree with the

recommendations made using the thermodynamic theory of aging (Gladyshev and Kurnakova, 1998; Gladyshev, 2001a).

Note that malignant tissue contains more water than normal tissue and resembles the young tissue, according to this gross index. It should be kept in mind, however, that the ratio of *intracellular water/extracellular water* in young and malignant tissue significantly differs. Further studies along these lines are of primary concern.

Thus, the data on the stability of the structures of cell membranes (j- 1-th hierarchy) and structures of cell aggregates (j-th hierarchy) do not contradict, at least qualitatively, the principle of substance stability. Highly stable structures of the lower (j - 1-th) hierarchy form lowly stable structures of the higher (j -th) hierarchy.

A well-known fact in the sphere of sociology concerning family ties illustrates the relationship between the principle of substance stability and social hierarchy. Here, we have in mind the substance of any hierarchy, such as a hierarchy of organisms, groups of organisms, etc. The stronger the love and mutual understanding between *a* couple, the less time they spend "outside the family". Such spouses do not have the desire, power, or time for this. This seems surprising. The thermodynamics of complex systems can be applied here as well. It goes without saying that in this example the thermodynamics of social hierarchy and the concept of sociological thermodynamic potential should be used (Gladyshev, 1978, 1997, 2001b). Hence, the principle in question is applicable to all hierarchies, including the molecular and supramolecular structures for which it was formulated.

These facts confirm the author's point of view (Gladyshev, 2000) that feedback between all hierarchic levels of the bioworld is based on thermodynamics. These feedbacks can he schematically presented as a sequence: *ecosystems → populations → organisms → cells → supramolecular structures → proteins and some other macromolecules →DNA.*

It would be of interest to study a possible application of the principle of substance stability to the development of new approaches to general problems of evolutionism (*Evolyutsionnaya…*, 2000; Brooks, 2001). Specifically, its greater promise may lie in its ability to reveal new general mechanisms of higher nervous activity, such as mechanisms of self-regulation under stress conditions (Sudakov, 2000).

It may be advisable to call the principle of substance stability "the feedback principle" and apply it to all three worlds of K. Popper (1984). Thus, the world of our mind or spirit, World 2, and the world of culture, World 3 (due to feedback between them), being higher hierarchic levels may rejuvenate the lower hierarchic levels of our material world, World 1. Undoubtedly, such "intellectual" rejuvenation prolongs our life and the life of human society. Note that interrelations in Popper's worlds are certainly realized through actual mechanisms inside our material world (Hayflick, 1996).

It appears that the principle of substance stability is applicable, despite some limitations, which apply to all hierarchies, both organic and inorganic.

Application of the Principle of Substance Stability to Structural Hierarchies of Inorganic Matter

The formulation of the principle of substance stability is related to the following thermodynamic postulate: each particle (unitary structure) of any hierarchic level has a certain limited possibility of being involved in interactions with particles (unitary structures) of the same and other hierarchic levels.

Thus, the atom involved in the formation of a relatively fast (stable) chemical bond(s) and, thereby, having already used its main "contact" energy capabilities can only form relatively weak intermolecular bonds. And, on the contrary, the same atom involved in the formation of a relatively weak chemical bond(s) can form fast (stable) intermolecular bonds. Note that our principle agrees with the earlier concept of L. Pauling based solely on the energy possibilities of the atoms involved in the formation of various chemical bonds (Pauling, 1947; Tulub,1989).

Rigorous substantiation of the formulated principle is complicated since it is impossible to determine the absolute values of functions of the state, such as Gibbs' function (G, G^*), Helmholtz' function (F, F^*), and enthalpy (H, H^*) of a simple or complex (*) system (Sychev, 1986; Gladyshev, 1996; Gladyshev and Kurnakova, 1998). However, all these functions can be used in a possible application of the principle for qualitative and semi quantitative investigation of the thermodynamic behavior of hierarchic systems.

It is easy to verify that the principle of substance stability can be applied to monotypic atoms. Let us compare the stability of atoms of rare (inert or noble) gases and their chemical compounds. Assume that the stability of the atoms of inert gases as structures of atomic hierarchy is determined by the first potentials of their ionization, U_I. In a sequence of He, Ne, Ar, Kr, Xe and Rn, U_I, gradually decreases from 24.6 eV (He) to 10.8 eV (Rn). At the same time the stability of chemical compounds formed by inert gases is known to decrease in the sequence Rn, Xe, Kr and Ar. Thus, the decrease in stability of atoms ($j - I$-th, lower hierarchy) in this case is accompanied by the increase in stability of their chemical compounds (j-th, higher hierarchy).

Note that such patterns are sometimes revealed when comparing the stability of sequences of monotypic atoms and their nuclei. It was already mentioned that the stability of atoms of inert gases gradually decreases in the sequence He, Ne, Sr, Kr, Xe and Rn. At the same time, the stability of nuclei (characterized by specific energy of nuclones, E/A, MeV) increase in the sequence He, Ne and Ar, although upon transition to Ar, Kr, Xe and Rn the value of E/A decreases, but not significantly. Thus, again, when considering the stability of monotypic structures of the nuclear (lower, j- 1-th) and atomic (j -th) hierarchies, it is sometimes pertinent to speak, with some reservations, about the above-mentioned postulate.

Thus, the principle of substance stability may be useful for studying the evolution of matter at many (structural) hierarchic levels.

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