WP7: Supercomputer simulations of bio-molecules and systems

1. Main activities and results

Task 7.1: ***Simulations of hIFNγ interactions.*** A computer model of the human interferon gamma (hIFN-γ) binding to its cellular receptor was proposed. The role of the high charge density of hIFN-γ C-termini for the cytokine activity was revealed. The hypothesis for a third participant in the process – the heparin sulphate, was investigated. As a ***new task*** within the current project, a computer model of heparin will be developed for a detailed study of its binding to hIFN-γ and of the mechanism of its anticoagulant action. *[Leandar Litov, Peicho Petkov, Petko Petkov, Nevena Ilieva]*

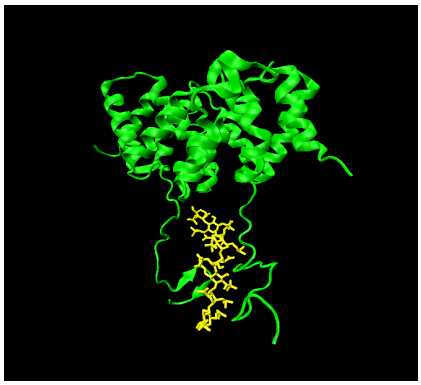

Fig. 1 *hIFN-γ – dp8 complex.*

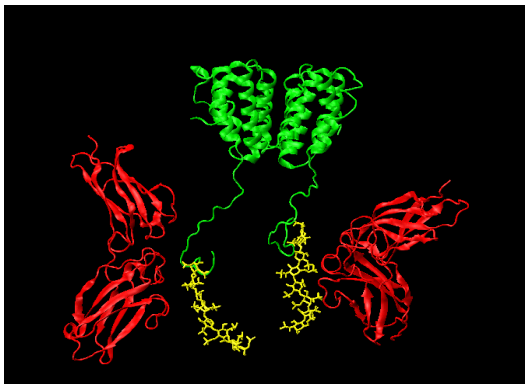

Fig. 2 *HS participation in the hIFN-γ – hIFNγRα complex formation*

In order to find a mechanism for inhibition of hIFN-γ biological activity, the possibility to synthesize a mutant form, which does not cause biological response in the cell was investigated. By means of a MD computer model, the alterations in the tertiary structure, caused by mutations of aminoacid residues 86-88 in the molecule of hIFN-γ were investigated. [Leandar Litov, Elena Lilkova, Peicho Petkov, Petko Petkov, Nevena Ilieva]

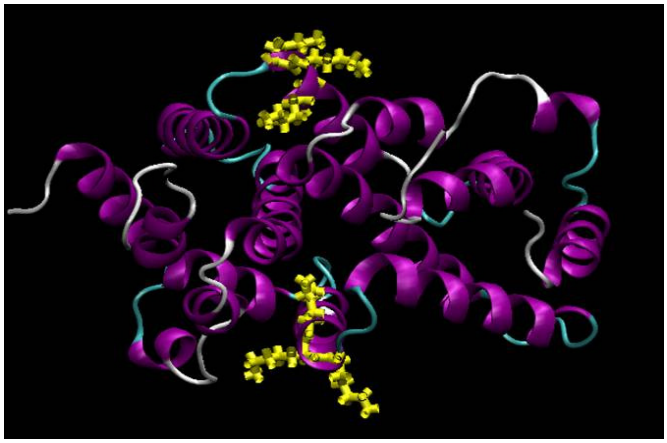

Fig. 3 Mutant *hIFN-γ form.*

Task 7.2: ***Structure and dynamics of the peptidyl transverse centre in RNA.*** The structure and dynamics of the peptidyl transverse centre of the RNA were investigated. The efforts were directed towards the selection of parameters and conditions that are appropriate for modeling of the dynamics of large biomolecules in water with classical MD methods. Non-conventional additions to the force-field that correspond to the specific nucleobases in the transport RNA are being tested. As a new task the creation of a computer model of an elementary aminolysis act during ribosome elongation stage is envisaged, which will enable investigations on the impact of the mechanical force applied on the tetrahedral carbon atom. [Miroslav Rangelov, Peicho Petkov, Petko Petkov]

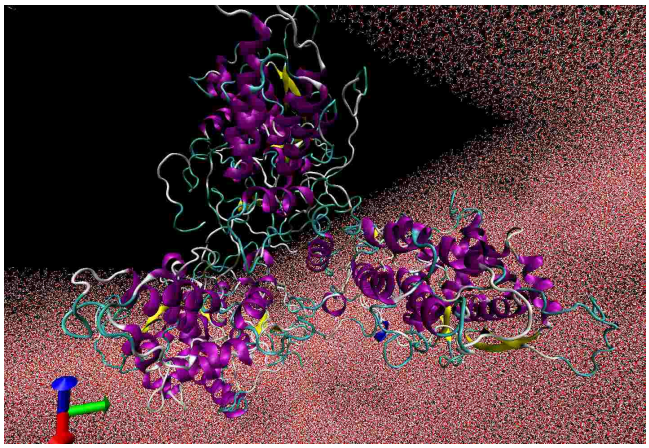

Fig. 4 Structure of the investigated peptid, with some of the water molecules shown.

***Task 7.3*: Modelling the process of protein bond formation in ribosome.** Based on the performed computations, a complete scheme of the possible reaction mechanisms of the protein bond formation in ribosome was constructed, a paper being in preparation. *[Miroslav Rangelov, Georgi Vayssilov]*

2. Publications, attributed to project DO 02-115/08

a) published:

b) accepted for publication:

[LLPPM_09a] E. Lilkova, L. Litov, P. Petkov, P. Petkov, S. Markov, Computer simulation of human interferon-gamma mutants, Heron Press, Sofia

[LLPPMI_09a] E. Lilkova, L. Litov, P. Petkov, P. Petkov, S. Markov, and N. Ilieva, Computer simulations of human interferon-gamma mutated forms, Proceedings of BPU7, Alexandroupolis

c) submitted for publication:

d) in preparation:

[LPPMI_09p] L. Litov, P. Petkov, P. Petkov, S. Markov, and N. Ilieva, Understanding of interferon-gamma binding

[RV_09p] M.A. Rangelov, G.N. Vayssilov, Catalysis by Vicinal Hydroxyl in 1,2-Diol Monoester Aminolysis: Implications for the Ribosome Mechanism

3. Talks and presentations

[1] L. Litov, Computer-aided drug design (plenary talk), Bulgarian-Japanese Symposium „Genomics and Proteomics in Personalized Medicine“, Sofia, March 19-22, 2009

[2] P. Bambova, Free energy of salvation of amino acids, CCP 5 Summer School on Methods in Molecular Simulation, England, July 2009

[3] D. Grancharov, Studying of Viscum Album Agglutinin binding with Zeatin, N6-adenin and N6-benzyladenin with DOCK 6.2 (poster), CCP 5 Summer School on Methods in Molecular Simulation, England, July 2009

[4] E. Lilkova, Computer simulation of human interferon-gamma mutants, Meetings in Physics, Sofia University, March 2009

[5] D.Grancharov, Studying of protein binding with ligand with DOCK 6.2, 7th Students Conference of the Balkan Physics Union, Bodrum, Turkey, September 2009

[6] P. Petkov, Computer simulations of human interferon-gamma mutated forms, 7th General Conference of the Balkan Physics Union, Alexandroupolis, Greece, September 2009

[7] L. Litov, High-performance computing, large-scale simulations and drug design (plenary talk), Federation of European Biochemical Societies, Sofia School of Protein Science "From basic research to drug design", Sofia, September 2009

[8] D. Grancharov, Studying of Viscum Album Agluttinin binding with Zeatin, N6-adenin and N6-benzyladenin with DOCK 6.2, Federation of European Biochemical Societies, Sofia School of Protein Science "From basic research to drug design", Sofia, September 2009

[9] P. Petkov, Understanding of interferon-gamma binding,1st National Conference with International Participation on Biomedical and Bioprocess Engineering, Sofia, December 2009

4. Other activities

[1] Establishment of the foreseen infrastructure: The establishment of a computer cluster for high-performance parallel calculations is foreseen in the project. It will be basically used as a test platform for parallel-program codes for massive calculations at the BlueGene/P supercomputer as well as for users' training in parallel calculations. After preliminary investigations, the cluster-project documentation has been prepared. A tender has been opened under the law of public errands for purchasing the cluster. The decision will be taken after disclosing the submitted offers, which is foreseen for 06.01.2010. The necessary equipment for a computer class with 12 workstations has been purchased, dedicated for training of students and users, as well as for development and application of high performance parallel-calculation codes. The room for the computer class is being prepared.

[2] Dedicated software: Packages for simulations of complex atomic and molecular systems within both classical (molecular dynamics) and quantum physics have been installed. Because of the BG/P architecture and software specificity, the adaptation of existing packages and the ensuring of their scalability are non-trivial effort- and time-consuming tasks. So far, the molecular dynamics packages NAMD and GROMACS and the codes for simulation of quantum systems CPMD and CP2K are successfully installed and tested.

[3] Organizational activities

- Workshop for work packages WP5, WP6 and WP7

- Agreement for coordination of the project expenses (re-allocation of part of the travel money for necessary for the completion of the project purposes equipment)

[4] Lecture courses

- L. Litov, Programming in UNIX environment

- L. Litov, Simulations of bio-molecule interactions

- A. Proikova, Introduction in high-performance computing

[5] Successfully defended 3 bachelors theses (P. Bambova, D. Grancharov, E. Lilkova)

[6] Popularization of the project objectives and results

- Nevena Ilieva, Physics and Life Sciences: towards a common future, Science Days 2009, Language School "Prof. Dr. V. Zlatarski", Sofia