

The anticipated 700 MHz NMR instrumentation is an optimal compromise of cost-effective, high-field and high-resolution NMR equipment suitable for biomolecular studies.

The UPAT's 700 MHz NMR (SEE-STRUCT Module) with a cryogenically cooled probe for enhanced sensitivity and four channels, in concert with uniformly or selectively enriched recombinant proteins (in ^{13}C , ^{15}N and ^2H), allows the set up of various applications in the field of structural biology and drug design. Such an instrument will permit the:

- High-resolution, comparable to X-ray, structure determination of protein drug-targets with molecular weight above 10 kDa, and atomic-level insight in protein and protein-protein/drug complexes dynamics, interaction and determination of binding affinity.
- Novel NMR experiments for fast acquisition of 3D, 4D, 5D, nD, using automated spectra collection and analysis of projections of N-dimensional spectra (K. Wüthrich et. al. Proc Natl Acad Sci USA 2005, 102;10876-10881). This application measures the information content of high dimensional spectra in low dimensional projection spectra, which results in a drastic reduction in acquisition time (while the acquisition of a complete set of heteronuclear 2D/3D experiments requires up to 3 weeks for a protein sample of 80-100 residues, this technique requires less than a week).
- Coupled fast acquisition and automated assignment techniques with unsupervised structure determination of proteins that reduces the time of the entire procedure from months to weeks.
- Time-resolved kinetics and fast acquisition of 2D fingerprint, diagnostic, ^1H - ^{15}N HSQC spectra (~1 sec), eventually crucial for monitoring protein-protein/peptide/small-molecules transient complexes, folding/unfolding processes and mechanistic studies, protein-drug screening applicable in drug-design process.
- Use of reduced protein amounts and investigation of low concentration protein samples (since numerous proteins exhibit low expression yields, while others tend to homo- or hetero-oligomerize or aggregate in medium to high concentrations, i.e. >0.4-0.6 mM).

The UPAT's existing 400 MHz NMR instrument, will still be exploited in the fine-tuning of the peptide/protein sample experimental conditions and the characterization of the small molecules. The 700 MHz NMR machine will be dedicated to high-resolution structural studies, high-throughput protein samples and screening of drug candidates and structure-based drug-design efforts.

Additionally, it will allow researchers from the entire Greek Academia or Industry and all the

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other Southern-East Europe countries (like Bulgaria, Turkey or others) to have access to this modern instrumentation. Access will be provided not only on a protein sample screening basis prior to NMR studies or X-ray crystallography, but also on a joint collaboration basis.

It will also allow the researchers working with small molecules to perform daily walk-in analysis of their samples. Finally, and even more importantly, cutting-edge structural biology projects will be eventually performed.