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## STRUCTURE ANALYSIS OF MOLECULAR SYSTEMS IN THE INSTITUTE OF MACROMOLECULAR CHEMISTRY OF THE CZECH ACADEMY OF SCIENCES

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### Abstract

The paper describes shortly the history of the Institute of Macromolecular Chemistry of the Czech Academy of Sciences and activities of the departments involved in X-ray and neutron structure analysis of materials.

### History background

**Academy of Sciences.** In spite of the fact that the first University in Middle Europe was founded by Charles the fourth in Praha, and Kepler wrote his discussions about the crystalline state of matter in Praha, the natural sciences had no impact on economy. Also the Czech Royal Society for Sciences founded in 1784 was a club of several scientists. The following “Czech Academy of Sciences and Arts” founded in 1790 had a better economical background, however without any chances for serious support of research. Thus, the scientific research in the Czechoslovak Republic between the World Wars (1918-1938) took place at several traditional state and technical universities and some applied research laboratories at huge industrial complexes, as “ŠKODA industrial factories” (machines, technological constructions), “Mannesmann steel works”, BA•A factories in Zlín, etc.

After the Second World War, all industrial states understand that their future and economy potential depends mainly on their success on the development of science and technology research. It was reflected in dramatic increase of new research institutes and universities in all industrial countries in the world in the fiftieths of the 20th century. In Czechoslovakia it was reflected in support of many industrial laboratories (resort institutes) and in establishment of the Academy of Sciences of the Czechoslovak Republic in 1952. In spite of very limited contacts with the international community because of political reasons (iron curtain), the Academy developed into an internationally well recognized institution represented practically in all international institutions (UNESCO, ISCU, IAEA, WHO, IUCr, etc.), organizing the largest scientific conferences, producing several hundreds PhD students a year and awarding the title Doctor of Sciences (Dr.Sc.) for scientists with at least 60 original papers in internationally accepted journals.

Prof. Jaroslav Heyrovský – director of the Polarographic Institute of the Czechoslovak Academy of Sciences was awarded the Nobel price for Chemistry in 1959.

In 1989, Academy included 61 Institutes in the Czech Republic and 37 Institutes in Slovakia with 7 thousand scientists and 4 thousand other employees producing several thousands of papers in impacted journals. After division of Czechoslovakia, the Czech part of the Academy was re-named to the Academy of Sciences of the Czech Republic. Nowadays, the Czech Academy of Sciences has 54 research institutes with about 3 500 scientists and 3 000 other workers.

**Crystallography.** Since 1993, the Academy organizes also scientific societies (to this date, it is 71 societies with 40 – 3000 members). One of them is the Crystallographic Association with 420 members. Its origins date to 1953, when the development in the use of X-ray techniques was influenced by a committee of the Academy lead by Prof. Adéla Kochanovská. At this time the X-ray technology was introduced into many industrial companies and research institutes. As far as the organization of science, she initiated a series of one-day meetings called „Discussions on Recent Topics in the Structure of Materials Using Ionization Radiation“. The series of these meetings (nowadays well known under a simple name „Discussions“ (Rozhovory) continues without any break already 58 years.

**Institute of Macromolecular Chemistry (IMC).** As far as the origins of the IMC, the committee of Academy for macromolecular sciences lead by V.Veselý a Otto Wichterle (both with long experience with polymer research in BATA research laboratories in Zlín) succeeded to convince the government to build a completely new institute devoted to macromolecular sciences at Petřiny. Their success was based on the discovery of several new polymer materials with industrial applications and on organization of the International Symposium on Macromolecular Chemistry in 1957 with 1100 participants from the whole world. Notice that the scientific tourism is a modern invention and at that time, symposia with more than thousand participants were something unusual.

The construction of the building started in 1960, and the scientists moved in 1962. The eight-floor glass building of the Institute of Macromolecular Chemistry with total 10 chemical and 10 physical departments was designed by the well known architect Prager in cooperation with scientists with long experience in chemical sciences (Otto Wichterle, Blahoslav Sedláček, etc.). The exceptional building of the Institute together with several other buildings of architect



Prager were approved by UNESCO as a cultural heritage and are now protected by national bodies.

The Institute has always been involved in international cooperation. Prof. Otto Wichterle, the director of the IMC initiated establishment of Macromolecular Division of the International Union for Pure and Applied Chemistry in 1967 and since then, the Institute organizes regularly two microsymbiosia under auspices of IUPAC each year.

### Diffraction studies in the Institute of Macromolecular Chemistry

#### Period 1960 – 1970

Karel Toman, the head of the Department of Diffractometry belonged among the founding member of the Institute of Macromolecular Chemistry with total 10 chemical and 10 physical departments. The original staff of the Diffraction Department – Josef Baldrian (crystallinity of polymers), Karel Huml (structure determination), Drahomíra Hlavatá (structure determination), Karel Tichý (structure determination), Jiří Ječný (instrumental technique) was increased in 1967 by Jindřich Hašek (methods for structure determination) and in 1964 by Josef Pleštil (small angle scattering).

A good reputation of the department in the world can be seen e.g. on the fact that the “Symposium on Structure Determination by X-ray Diffraction” organized several weeks after the invasion of Soviet troops into Czechoslovakia was visited by 140 scientists, including two future Nobel price winners. Interestingly, the participants occupying full capacity of all lecture rooms in the Institute were from western countries only – the participants from countries of the Warsaw treaty did not get exit visa to Czechoslovakia at this time. Karel Toman and Karel Tichý emigrated early in 1969.

#### Scientific orientation

##### *Structure determination of molecular systems*

- Poly-iodine complexes
- Catalysers of polymerization reactions and intermediate complexes
- Structures of macrocyclic polyethers

##### *Material properties*

- Crystallinity of polymers
- Phase separation and micro-inhomogenities in polymer blends

#### Period 1970 – 1993

Dr. Karel Huml became the head of the department after his return from a two-year post-doctoral stay in Canada in the laboratory of Dr. Ahmed and organized several large international conferences under auspices of the International Union of Crystallography (IUCr). He worked permanently in the IUCr committees and served many years as a president of the European Crystallographic Association.

In period 1970 - 1993, the laboratory led or hosted several PhD students - Jindřich Hašek (methods for structure determination), Drahomíra Hlavatá (structure determination), Josef Pleštil (small angle scattering), Bohdan Schneider (amino acids, nucleic acids, PDB), Jindřich

Symerský (structure determination), Miloš Steinhart (small angle scattering), Jiří Šolér (structure of bacteriophage), Jaroslav Vojtěchovský (structure determination – myoglobin structures).

Cooperation with University of Amsterdam NL, University of York UK, University in Bari IT, Dubna SSSR, IUCr and European Crystallization Committee.

#### Scientific orientation

- Structure systematics of crown ether complexes and conformation analysis of large macrocyclic compounds.
- Structure interpretation of photochromic properties of compounds belonging to sydnone ring derivatives and to dihydropyridine-derivatives
- Structure of organic conductors containing CTNQ, TFF, etc.
- New methods for phase problem solution based on distribution fitting of seminvariants
- Structure determination of cyclic oligomers isolated from classical polymer materials
- Structures of various metabolite products.
- Short peptides used in pharmacy as cleavable linkers for selective transport of the active substance to the target tissue by advanced drugs of new generation.
- Structure determination of bacteriophage S<sub>d</sub> with molecular weight 110 000 kDa

#### Period 1993 – 2010

In the period 1993 - 2010 the department was divided into the laboratory for small angle X-ray and neutron scattering (J.Pleštil) and the laboratory for molecular structures (J.Hašek).

The group of small angle scattering have at present 6 people (Josef Baldrian, Alexander Jigounov, Josef Pleštil, Miloš Steinhart, Borislav Angelov, and technician Hana Šandová). Cooperation Dubna, ELETTRA Trieste, ILL Grenoble.

#### Scientific orientation - Material properties

- Colloid systems
- Hybrid nanocomposites
- Crystallinity of polymers
- Self assembly of amphiphilic block copolymers
- Phase separation and micro-inhomogenities in polymer blends
- Measurement of phase separation of polymer blends under high pressures

The department for structure determination of macromolecules specialized for diffraction studies of large bio-molecular complexes and on interactions of biomolecules with synthetic polymers. At present, the laboratory has the following scientists - Jan Dohnálek, Jarmila Dušková, Jindřich Hašek, Petr Kolenko, Tomáš Koval (PhD student), Tereza Skálová, and Andrea Štěpánková (PhD student). PhD students who learned structure determination of bio-macromolecules in this period were Eva Buchtelová (Vondráčková), Jan Dohnálek, Ondřej Hartman, Petr Kolenko, Tomáš Koval, Ivana Kutá-Smatanová,



Hana Petroková, Ondřej Rázga, Tereza Skálová, Andrea Štěpánková.

### Scientific orientation

Static and dynamic aspects of catalysis following from X-ray structure determination were discussed for several enzyme classes treated in our laboratory - differently mutated HIV proteases in complex with a series of inhibitors, galactosidases, immunoglobulins, chitinases, oxidases, RNases, glycosylation, differently hydrated valinomycin complexes, and development of the Polymer Structure Database.

- Aspartic proteases - Structure determination of twelve HIV-1 protease mutants in complex with a series of tetrapeptide inhibitors evidences that the affinity of inhibitors to the binding site is highly correlated among others also to the elasticity of the binding tunnel and mobility of flaps in addition to the classically discussed enthalpy terms [2,4,5,6,8,9]. The X-ray diffraction analysis showed a self-inhibition of HIV protease after finishing its function in the virion particle [3]
- Thermal dependence of catalytic activity of proteins - structure of a cold active  $\alpha$ -galactosidase and its complexes [7]
- Structure and function of a new trimeric form of laccase [13]
- Structure and function of immunoglobulins, glycosylation [12]
- Practical impacts of the genetic mutations of pyridoxal 5'-phosphate dependent enzymes in clinical practice [14]
- Theory of protein surface modifying agents and its use in crystallization of biological macromolecules [11]
- Structures of valinomycin complexes in different degree of hydration showed new supposed mechanism for passive transport of small molecules and ions through membranes
- Small molecular markers [10]
- Systematic analysis of interactions between synthetic polymers and proteins
- Development and maintenance of the Polymer Structure Database [1]
- New polymer screens for protein crystallization [15]

Organization of many conferences. Number of regional, bilateral and European projects. Cooperation is di-

rected mainly to NOVOZYMES DK, Oxford University GB, York University GB, INRA FR, ESRF Grenoble FR, ELETTRA Trieste IT, University of Manchester GB, BESSY, University of Colorado USA.

### Conclusion

Structure analysis of materials by X-ray radiation belongs already 40 years to the main streams of research in the Institute of Macromolecular Chemistry AV ČR. The topics solved cover all topics in macromolecular sciences accessible by X-ray techniques, i.e. structure determination of molecular complexes of any size at atomic resolution by X-ray diffraction, structure determination supramolecular systems on nanoscale by X-ray scattering, new methods for structure determination, crystallization of bio-macromolecules, structure systematics, the analysis of a function of complex systems and the relevant practical applications.

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