

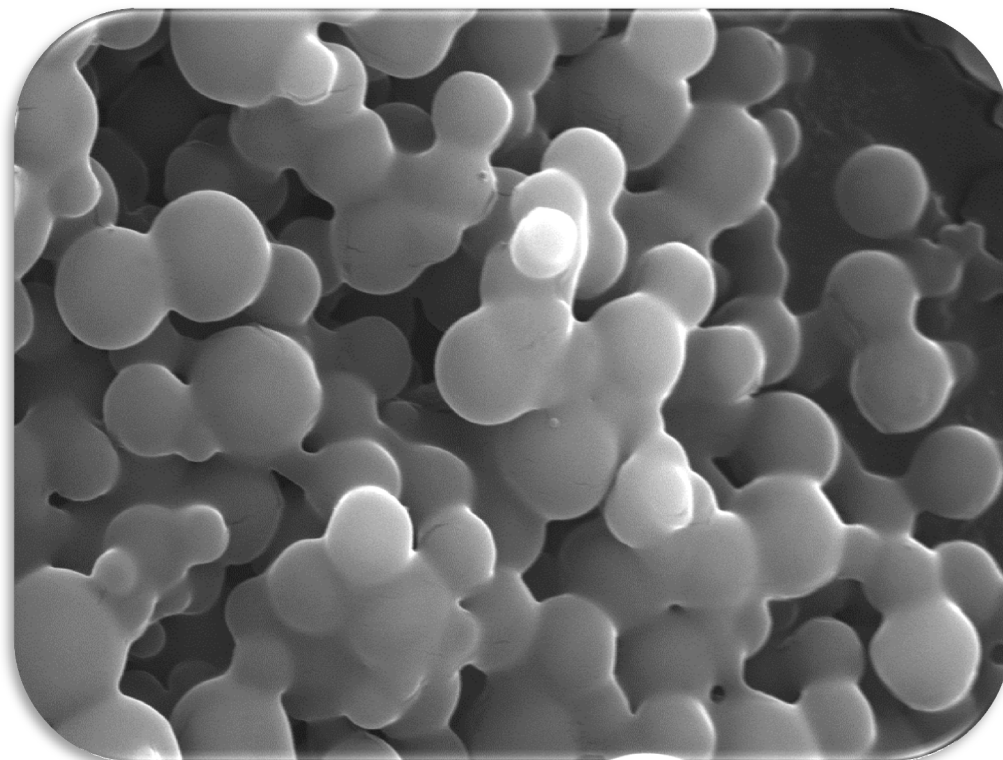
INSTITUTE OF MACROMOLECULAR CHEMISTRY CAS



WORKSHOP

CAREER IN POLYMERS X

PRAGUE, 22-23 JUNE 2018



Draslovka

 The Czech Academy
of Sciences
Strategy AV21
Top research in the public interest

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HEYROVSKÉHO NÁM. 2, 162 06 PRAGUE 6, CZECH REPUBLIC

BOOK OF ABSTRACTS

WORKSHOP CHAIRMAN

LIBOR KOBERA

Photo on the Cover: K. C. Loureiro, SEM of the nanoparticles before spray -drying processes (from lecture 1).

EDITORIAL INFORMATION

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WORKSHOP CAREER IN POLYMERS - NEW DIMENSION OF PRAGUE POLYMER MEETINGS

The Institute of Macromolecular Chemistry, Czech Academy of Sciences has become an important center of European polymer research since its foundation in 1959. Currently, it encompasses virtually all branches, directions and trends in contemporary polymer science. Besides, the Institute became famous as an organizer and venue of many congresses, conferences, world symposia, microsymposia, discussion conferences and summer schools devoted to polymer science in general and various special aspects of polymer chemistry, physical chemistry, physics and technology, in particular. The specialized symposia became known as Prague Meeting on Macromolecules (PMM).

In 2009, a new dimension of these Prague polymer meetings emerged. Immediately after the 73rd PMM Conference, a special workshop named “Career in Polymers” was organized under the auspices of the Central and East European Polymer Network, CEEP. It was aimed predominantly, but not exclusively, at young polymer scientists from Central and East European countries. The aim was to provide a forum for mutual contacts between young scientists just starting their career in polymers, to initiate their discussions with renowned scientists within the Institute, to promote polymer science and to show its charm and beauty. “Career in Polymers” covers all aspects of polymer science – polymer physics, polymer chemistry and applications of polymers especially in medicine, electronics, and as hybrid and composite materials. The recently established tradition of the Prague meetings for young scientists continues also in the year 2018. The workshop “Career in Polymers X” will include the closing seminar of the UNESCO/IUPAC Postgraduate Course in Polymer Science – the 22st run of the Course organized in the academic year 2017–2018. Furthermore, a part of this workshop is a meeting between young scientists and representatives from industry supported by Strategy AV21 “Top research in the public interest” and Draslovka a.s.



UNESCO/IUPAC COURSE IN POLYMER SCIENCE

The Postgraduate Course in Polymer Science has been organised by the Institute of Macromolecular Chemistry AS CR since the academic year 1996–1997 under the auspices of international organisations UNESCO and IUPAC and with financial assistance of the Czech Academy of Sciences. So far, 188 participants from the following 24 countries have attended the Course: Algeria, Bangladesh, Brazil, Bulgaria, Cameroon, China, Croatia, Egypt, Hungary, India, Iran, Kazakhstan, Macedonia, Mexico, Nepal, Poland, Romania, Russia, Serbia, South Africa, Ukraine, Uruguay, Uzbekistan and Vietnam.

The Course lasts 10 months and is comprised of about 50 hours of lectures in modern polymer science and of participation in all educational activities within the Institute. Most of the time, however, is devoted to experimental work on research projects under the supervision of senior scientists of the Institute. Active research is the keystone of the Course. Regularly, the participants report on progress of their research at working meetings of their teams and participate at seminars and technical meetings within the Institute. At the end of each run, a seminar in the form of an international workshop is organised, at which all the participants present their results.

Subsequent development of career of the Course participants shows, that completion of the Course has been very helpful to professional promotion of the graduates in their home countries. Co-operation with a number of them continues through joint projects with their home laboratories. At least 34 graduates have commenced a Ph.D. degree programme at Czech universities in cooperation with the academic laboratories; 11 of these doctoral students have successfully completed their respective Ph.D. degree studies; several others work as postdoctoral researchers at the Academy of Sciences of the Czech Republic. The graduates of the Course have published the results of their research in more than 500 papers in international scientific journals cited more than 10000 times and many communications at international meetings. Detailed information on the Course can be found at http://www.imc.cas.cz/en/umch/kursy_unesco_iupac.htm.

At the General Assembly of the International Union of Pure and Applied Chemistry, held in Beijing, China in August 2005, the organisers of the Course were awarded the 2005 IUPAC-Samsung Education Prize by the President of the Union, the Prize was sponsored by the Samsung Company.



INTERNATIONAL UNION OF
PURE AND APPLIED CHEMISTRY



The Czech Academy
of Sciences

PROGRAM

22 June 2018

9:00	Welcome
9:20	K. C. Loureiro
9:40	K. A. Milakin
10:00	L. N. Khatiwada
10:20	T. Urbaniak
10:40	Coffee break + poster installation
11:00	A. Gupta
11:20	E. Böhmová
11:40	M. Tavares
12:00	G. Szpunar
12:20	V. K. Yadu Nath
12:40 – 14:00	Lunch
14:00	H. Beneš
14:20	D. Oleshchuk
14:40	A. Shatan
15:00	R. Balogh
15:20	Y. Panthi
15:40	Coffee break + poster installation
16:00	M. Konefał
16:20	Zs. Osváth
16:40	M. Gadek
17:00	L. J. C. Albuquerque
17:20	R. Konefał
17:40	Closing of the workshop
18:00	Banquet + Poster session

LIST OF CONTRIBUTIONS

MAIN LECTURES

- ML1** H. Beneš, R.K. Donato, S. Livi, J. Kredatusová, M. Perchacz, P. Ecorchard
IONIC LIQUIDS AND THEIR ROLES IN POLYMER HYBRIDS
AND NANOCOMPOSITES
- ML2** R. Konefał, J. Spěváček
STIMULI-RESPONSIVE POLYMER SYSTEMS INVESTIGATED
BY NMR SPECTROSCOPY

LECTURES

- L1** K. C. Loureiro, P. Severino, I. B. Lima-Verde, P. Štěpánek, A. Jäger
DRYING POLYMER NANOPARTICLES PREPARED BY
NANOPRECIPIATION
- L2** K. A. Milakin, J. Stejskal, M. Trchová, U. Acharya, J. Hodan, J. Kredatusová,
J. Hromádková, J. Pflieger, P. Bober
CONDUCTING COMPOSITE HYDROGELS
- L3** L. N. Khatiwada, M. Dušková Smrčková, J. Pflieger, J. Peter, D. Chmelíková,
D. Kubies, E. Chánová
WATER UPTAKE BY CROSSLINKED POLYURETHANE AND POLYUREA
COATINGS – A QCM METHOD
- L4** T. Urbaniak, D. Kubies, O. Pop-Georgievsky
SELF-ASSEMBLED MULTILAYER FILMS BASED ON NATURALLY-
DERIVED MATERIALS FOR TUNABLE PROTEIN RELEASE
- L5** A. Gupta, M. Kowalczyk, C. Martin, I. Radecka
BIOSYNTHETIC HYDROGELS WITH CURCUMIN-CYCLODEXTRINS
INCLUSION COMPLEX FOR WOUND MANAGEMENT APPLICATION
- L6** E. Böhmová, R. Pola, M. Pechar, M. Filipová, O. Janoušková, T. Etrych
PREPARATION AND IN VITRO EVALUATION OF POLYMER
CONJUGATES ACTIVELY TARGETED USING RGD-BASED PEPTIDES
- L7** M. Tavares, P. Bojarová, R. Konefał, V. Křen, T. Etrych, P. Chytil
GALECTIN-3-TARGETED HPMA-COPOLYMERS BEARING GLYCAN
LIGANDS
- L8** G. Szpunar, T. Etrych, L. Kostka
NANO GEL BASED DRUG DELIVERY SYSTEM
- L9** V. K. Yadu Nath, A. Ostafinska, M. Nevoralova, I. Fortelny, M. Slouf
BIODEGRADABLE TPS/PCL POLYMER SYSTEMS FOR MEDICAL
APPLICATIONS
- L10** D. Oleshchuk, V. Proks, Š. Popelka
PEPTIDE-MODIFIED SURFACES FOR BIOMEDICAL APPLICATIONS
- L11** A. Shatan, B. Zasoňska, D. Horák
ANTIBACTERIAL MAGNETIC NANOPARTICLES: DESIGN, SYNTHESIS
AND BACTERICIDAL EFFECT

- L12** R. Balogh, M. Danko, A. Eckstein-Andicsová, E. Kozma, Z. Tokárová
DESIGN AND SYTHESIS OF THIAZOLO[5,4-D]THIAZOLE OLIGOMERS
FOR ORGANIC SEMICONDUCTORS
- L13** Y. Panthi, J. Pflieger, B. Paruzel
A MEMRISTIVE BEHAVIOR OF Pi-CONJUGATED POLYMER
MOLECULARLY DOPED WITH ORGANIC ACCEPTORS
- L14** M. Konefał, A. Zhigunov
INFLUENCE OF DIP-COATING RATE ON PS-b-P4VP THIN FILMS
PROPERTIES
- L15** Zs. Osváth, B. Iván
POLY(N-ISOPROPYLACRYLAMIDE), AND THE SYNTHESIS
AND THERMORESPONSIVE BEHAVIOR OF ITS 3-
(TRIMETHOXYSILYL)PROPYL METHACRYLATE BASED COPOLYMERS
AND HYBRID GELS
- L16** M. Gadek, L. Matějka, B. Strachota
SMART AND SELF-HEALING PHOTSENSITIVE POLYMERS
- L17** L. J. C. Albuquerque, F. C. Giacomelli, E. Pavlova, P. Štěpánek, P. Černoč,
E. Jäger
ENVIRONMENTALLY RESPONSIVE BLOCK COPOLYMERS FOR
INTRACELLULAR DELIVERY OF HYDROPHILIC THERAPEUTICS

POSTERS

- P1** I. Romanenko, R. Sivkova, A. de los Santos, J. Svoboda, O. Pop-Georgievski
IMPACT OF THE HOFMEISTER SERIES ANIONS ON ETHYLENE GLYCOL
BASED POLYMER BRUSHES
- P2** I. Ivanko, J. Kredatusová, E. Tomšík
PHYSICAL-CHEMICAL PROPERTIES OF HYDRATED AND SELF-
ASSEMBLED POLY(3,4-ETHYLENEDIOXYTHIOPHENE) CHAINS
- P3** B. Johnston, D. Hill, M. Kowalczyk, I. Kwiecień, J. Rydz, I. Radecka
POLYHYDROXYALKANOATES (PHAS) OBTAINED FROM WASTE
PLASTIC MATERIALS TO PRODUCE BIOPOLYMERS FOR NOVEL
APPLICATIONS
- P4** I. M. Minisy, P. Bober, U. Acharya, M. Trchová, J. Stejskal
EFFECT OF SAFRANIN ON THE POLYMERIZATION OF PYRROLE:
MORPHOLOGY AND CONDUCTIVITY CONTROL
- P5** L. Kománková, M. Pařízek, H. Hlídková, M. Hrubý, M. Vetrík
THREE-DIMENSIONAL CARBON-BASED POLYMER SCAFFOLD
FOR BONE TISSUE ENGINEERING
- P6** K. Skleničková, D. Koloušek, M. Pečenka, D. Vejmelková, I. Růžičková
APPLICATION OF ZEOLITES IN FISH BREEDING AND THEIR EFFECT
ON NITRIFYING MICROORGANISMS

IONIC LIQUIDS AND THEIR ROLES IN POLYMER HYBRIDS AND NANOCOMPOSITES

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Ionic liquids (ILs) due to its non-toxicity, low volatility and broad variety of physicochemical properties have been intensively studied as additives for various polymers. In this contribution, the application of imidazolium and phosphonium -based ILs for preparation of epoxy-silica hybrids and polycaprolactone-layered double hydroxides (LDH) nanocomposites is demonstrated. Several roles of ILs are explored: as surfactants of nanofillers, as catalysts of hydrolysis-condensation and ring opening polymerization and as delaminating agents of layered 2D-particles (graphite and clays).

Acknowledgement: Financial support of the Czech Science Foundation (project 17-08273S) is gratefully appreciated.

STIMULI-RESPONSIVE POLYMER SYSTEMS INVESTIGATED BY NMR SPECTROSCOPY

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Stimuli-responsive (stimuli-sensitive, intelligent, or smart) polymers are polymer materials which, after small external stimuli, evidently change their physical or chemical properties. Smart polymers can be classified according stimuli they respond to such as: temperature changes, mechanical stress, light irradiation, ultrasonic treatment, application of external magnetic as well as electric field, changes of pH, ionic strength, addition of the chemical agents and presence of biomolecules and bioactive molecules. Stimuli-responsive synthetic polymer systems has attracted considerable attention due to wide range of applications, i.e. controlled drug delivery and release systems, diagnostics, tissue engineering and ‘smart’ optical systems, as well as biosensors, microelectromechanical systems, coatings, and textiles. Among the types of stimuli: temperature, pH and reactive oxygen species (ROS) responsive polymer systems were studied by NMR spectroscopy methods. In case of thermoresponsive polymers, when polymer chains are molecularly dissolved in a good solvent, changes (increasing or decreasing) of temperature result in insolubility (globular nanoparticles formation) of polymer chains, called temperature induced phase-separation. pH responsive polymers change properties such as: solubility, volume (gels), chain conformation as well as which bonds can cleavage upon changes in pH of environment. The ROS responsivity results in changes in solubility, hydrolysis, phase transition, and/or degradation of polymer chains.

Keywords: stimuli-responsive, phase transition, temperature, pH, ROS, copolymers, cryogel, PNIPAM, PVME, PEOx, ^1H NMR, ^1H spin-spin relaxation times, 2D NOESY

Acknowledgement: Support by the Czech Science Foundation (projects: 15-13853S; 13-23392S) is gratefully acknowledged.

DRYING POLYMER NANOPARTICLES PREPARED BY NANOPRECIPITATION

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Despite the high interest in the development of polymer nanoparticles, they present some drawbacks mostly related to the limited physicochemical stability which hinders the scaling-up and effective translation to the clinics. In this context drying techniques like freeze drying and spray-drying have been used to produce solid formulations of polymer nanoparticles and significantly increasing their physicochemical stability. In this work we evaluated and compared the capabilities of both techniques on the production of powders from polymer nanoparticles of poly(D,L-lactide-*co*-glycolide) (PLGA) prepared by nanoprecipitation. Powder samples were prepared by freeze drying and spray-drying using trehalose and lactose as drying protectants and characterized using dynamic light scattering (DLS) and scanning electron microscopy (SEM). In contrast to freeze drying the samples prepared by spray-drying resulted in transparent solutions after water resuspension. The DLS measurements of the solutions show that the PLGA nanoparticles prepared by spray-drying using trehalose or lactose retained the original distribution of hydrodynamic sizes in comparison to the freeze dried samples (Figure 1). The SEM images of the dry powders corroborated with the DLS measurements and show that the samples prepared by spray-drying are spherical in shape and homogeneously distributed whereas samples prepared by freeze drying are heterogeneous with undefined shape (inset, Figure 1). Therefore, spray-drying technique showed to be superior in the production of stable PLA nanoparticles in the solid state in comparison to the freeze drying technique.

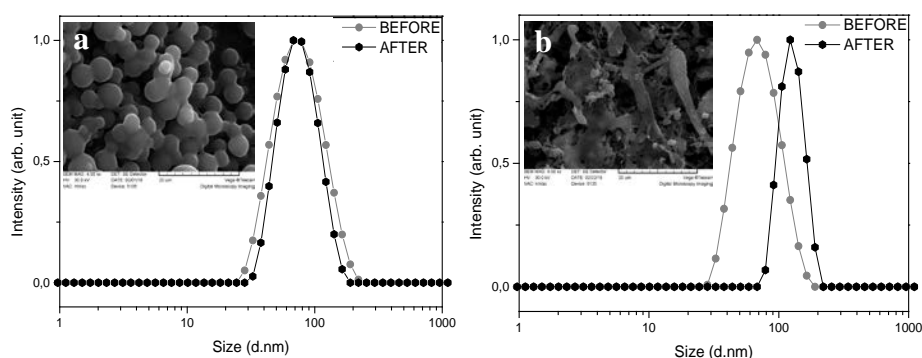


Figure 1. DLS and SEM of the nanoparticles before and after spray (a) and freeze (b) drying processes.

Keywords: nanoprecipitation, spray drying, freeze drying and polymer nanoparticles.

Acknowledgement: We would like to thank the UNESCO/IUPAC course and the Institute of Macromolecular Chemistry of Academy of Sciences of the Czech Republic.

CONDUCTING COMPOSITE HYDROGELS

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Conducting composite hydrogels are a promising class of materials which combine physico-chemical properties of conducting polymers, such as polyaniline and polypyrrole, with mechanical properties of a polymer stabiliser (e.g. poly(vinyl alcohol), poly(vinylpyrrolidone), gelatin). They can potentially be used as adsorbents, actuators, supercapacitors, drug delivery systems, tissue scaffolds, etc.

Conducting hydrogels can be conveniently synthesized by polymerization of aniline or pyrrole in the presence of a water-soluble polymer in a frozen medium (cryopolymerization).¹ This is an easy one-step approach for preparation of homogenous macroporous materials (Figure 1) with tunable characteristics. Depending on the potential application their conductivity, mechanical properties and morphology can be varied by changing a polymerization mixture composition and choosing an appropriate polymer stabilizer.

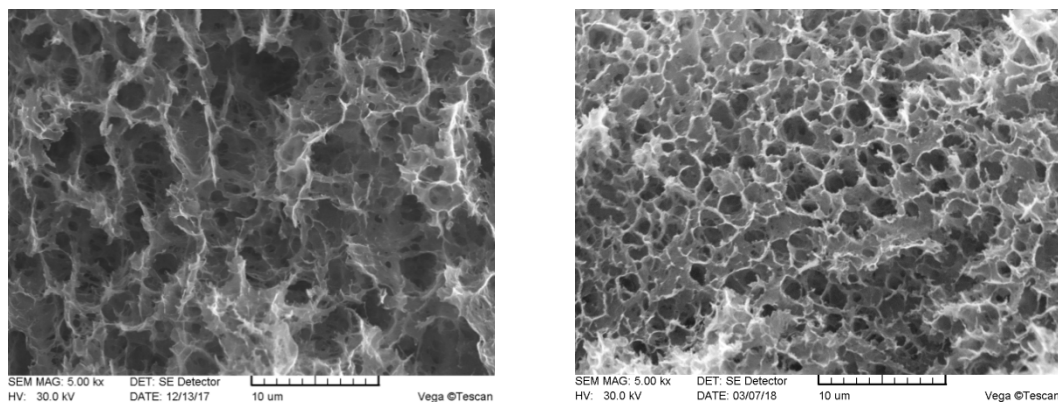


Figure 1. Scanning electron microscopy images of poly(aniline-*co-p*-phenylenediamine)/poly(vinyl alcohol) hydrogels.

Keywords: hydrogels, conducting polymers, conductivity, mechanical properties.

Acknowledgement: The authors wish to thank the Czech Science Foundation (16-02787S) for the financial support. One of us (K.A.M.) participated in the IUPAC/UNESCO-sponsored Postgraduate Course in Polymer Science 2017/18 organized by the Institute of Macromolecular Chemistry in Prague.

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WATER UPTAKE BY ULTRATHIN CROSSLINKED FILMS BASED ON POLYURETHANE AND POLYUREA STUDIED BY QCM

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Water diffusion into a cured network structure of high performance polymeric coatings always occurs under application conditions. Diffusing water influences the mechanical resistance and durability of coatings but also their adhesion to substrates even at very low concentration. The mechanism is related to formation of H-bonds which may influence the coatings in different ways: they may connect the network structure or hydrate the polar moieties of the network causing plastification, interact with residual diluent and diffuse further into the structure causing network relaxation – depending on network chemistry. To test the water uptake kinetics and equilibrium in very thin coatings we have set up a detection method based on quartz crystal balance monitor (QCM) capable of detection of very low mass changes, as low as 10^{-9} grams (i.e. nanograms) and adopted to studies of thin films under various humidity, pressure and temperature. In this contribution, we present the QCM apparatus designed for water uptake studies, and the results so far obtained with spin coated films.

We have studied water uptake by films based on polyurethane/polyurea chemistry and evaluated parameters such as network composition (hydrophilicity/hydrophobicity), crosslinked density, thickness of layers and external humidity level and pressure. The water uptake process revealed very fast initial uptake step and hysteresis behavior. The diffusion coefficients estimated using Crank model spanned the range of 1×10^{-9} to 5×10^{-10} cm^2/s and the equilibrium amount of absorbed water was surprisingly high around units of percent. The hysteresis effects were observed also in a parallel sorption-diffusion measurement done with a sorption balance and attributed to film morphology.

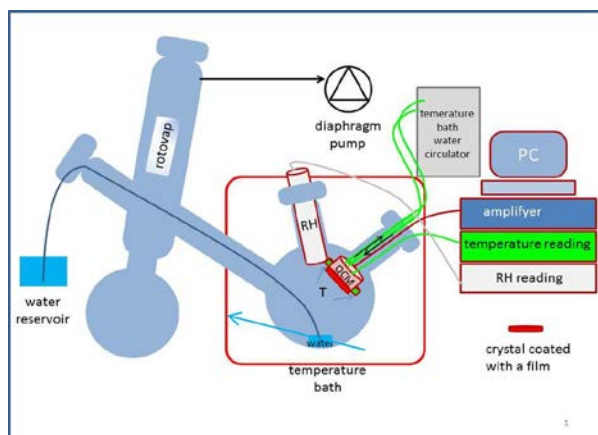


Fig. 1: QCM set-up for monitoring water uptake.

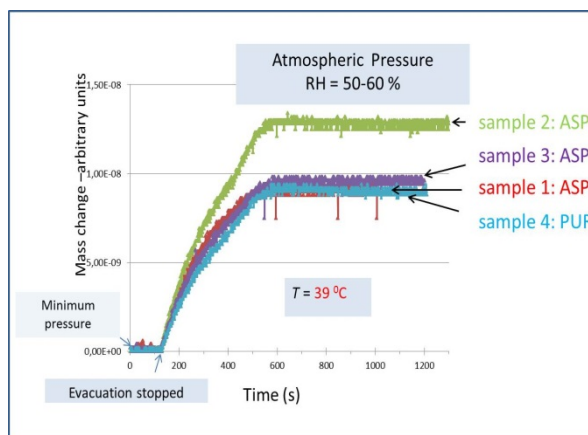


Fig. 2: Water uptake by thin films monitored by QCM.

SELF-ASSEMBLED MULTILAYER FILMS BASED ON NATURALLY-DERIVED MATERIALS FOR TUNABLE PROTEIN RELEASE

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Multicomponent coatings capable of a prolonged therapeutic agent release are attractive and widely studied variant of the surface modification. The ability to deliver various biologically active species in a controlled manner makes them suitable for implant and medical device modifications.¹ In our research, we evaluate multilayer thin films based on naturally-derived polysaccharides, quaternized chitosan (CMCH) and heparin (HEP). The CMCH/Hep multilayer film coatings were prepared by a layer-by-layer method (LbL) when the layer of the positively charged chitosan assembled with the negatively charged HEP layer at pH 7.4 preferable for incorporation of biological factors. The CMCH/Hep assemblies were loaded with the cytokine stromal cell-derived factor 12 (CXCL12) known as a chemotactic factor for cells of immune response. The protein attachment to the heparin molecule occurs via unspecific electrostatic interactions of the positively charged CXCL12 and the negatively charged Hep as well as via natural affinity of this cytokine to Hep.² CXCL12 was introduced into the LbL system in two ways: a) as a separated protein CXCL12 layer or b) as a Hep layer enriched with CXCL12 in a form of their co-solution. The successful deposition of the particular polyelectrolyte layers was confirmed by surface plasmon resonance, changes in the coating thickness during the deposition were monitored with spectroscopic ellipsometry. The surface topography of the obtained films was assessed via atomic force microscopy mapping. The CXCL12 release from the coatings was evaluated using ELISA method and its biological activity was verified in *in vitro* cell migration studies using human T lymphoma cell line. Nano-sized ultrathin films exhibited distinctive surface morphology, which indicates occurrence of the film component reorganization during the deposition, and suggests dynamic nature of the assembly process.³ The obtained coatings proved to be suitable for use as protein reservoirs.

Keywords: layer-by-layer coating, protein delivery, ultra-thin coatings, cell migration studies

Acknowledgement: Research was carried out as a part of 22nd UNESCO/IUPAC Course in Polymer Science, and supported by the Ministry of Education, Youth and Sports of the Czech Republic, National Sustainability Program II (Project BIOCEV- FAR LQ1604), and by the BIOCEV project (CZ.1.05/ 1.1.00/02.0109)

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BIOSYNTHETIC HYDROGELS WITH CURCUMIN-CYCLODEXTRINS INCLUSION COMPLEX FOR WOUND MANAGEMENT APPLICATION

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Natural products like curcumin (CUR) are becoming more popular for wound management applications^{1,2} and are less likely to develop resistant strains.² However, hydrophobicity of CUR limits its certain biomedical applications. This can be overcome by inclusion of CUR in carriers like cyclodextrins (CDs).³ In the present study, an attempt has been made to form water soluble inclusion complex (IC) of CUR in hydroxylpropyl beta-cyclodextrin (HP β CD) using solvent evaporation method and loading it in cellulose based biosynthetic hydrogels to produce antimicrobial wound dressings.

Bacterial Cellulose (BC) hydrogels were obtained from *Gluconacetobacter xylinus* ATCC 23770 using the protocol reported previously⁴. Padded dry BC pellicles were loaded with 5% aqueous solution of inclusion complex (IC) under constant agitation. These biosynthetic hydrogels (8mm disc diameter) were tested for antimicrobial activity against *Staphylococcus aureus* (*S. aureus*), Gram positive opportunistic microbes, at 24hrs using disc diffusion assay. Morphological study revealed that when BC was immersed in CUR-HP β CD solution, IC was physically trapped in the BC fibers (Fig. 1). Disc diffusion results revealed that at 24hrs, CUR-HP β CD-BC exhibited antimicrobial activity (Fig. 2) against the tested strain of *S. aureus*. These results suggest that CUR-HP β CD-loaded BC hydrogel is a promising candidate in wound management due to its moisture promoting, biocompatible and antimicrobial nature.

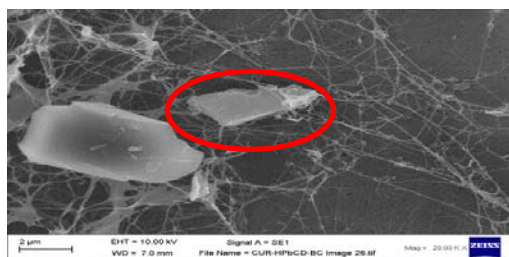


Figure 1. SEM image of IC physically entrapped (circled) in BC fibres in CUR-HP β CD-BC.

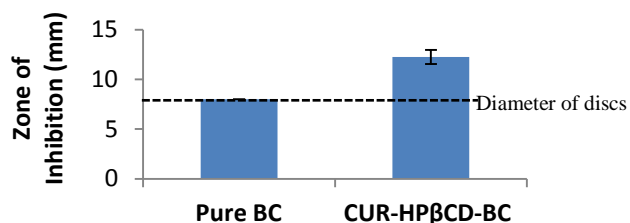


Figure 2. A graph to represent ZOI for pure BC and CUR-HP β CD-BC against *S. aureus* ($n = 8$; error bars = S.D.).

Keywords: Antimicrobial; bacterial cellulose; hydrogel; curcumin; wound healing

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PREPARATION AND *IN VITRO* EVALUATION OF POLYMER CONJUGATES ACTIVELY TARGETED USING RGD-BASED PEPTIDES

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RGD-based peptides are well known as structures capable of targeting to tumor neovasculature. Recently, actively targeted polymer cancerostatics using linear RGD-based peptides has been already described by our group.¹ The main aim of the present work is to compare polymer carriers targeted by linear peptide and by branched form of RGD.

This work is focused on preparation of polymer conjugates based on copolymers of *N*-(2-hydroxypropyl) methacrylamide with comonomers bearing various RGD-based peptides and fluorescent label cyanine 5.5 attached to the main polymer chain. First, copolymers containing reactive thiazolidine-2-thione groups with narrow distribution of molecular weights were prepared by RAFT polymerization using dithiobenzoates as chain transfer agents. RGD-based peptide sequences were prepared by standard Fmoc solid phase peptide synthesis using Tenta gel Rink amide resin. Fmoc-NH-PEG(4)-COOH was used as a linker between the peptide and the polymer chain. Coupling of the copolymer with the dye and the peptide via amino groups in an aqueous buffer at pH 8 was monitored by HPLC. The synthesized peptide-polymer conjugates were characterized by SEC. Targeting activity was verified *in vitro* using human umbilical vein endothelial cells (HUVEC) as $\alpha_v\beta_3$ integrine positive cell lines. Comparison of each conjugate in terms of endothelium cells targeting efficiency was also monitored. The intended application of these polymer conjugates is selective fluorescent labeling of tumors for endoscopic surgery head and neck carcinomas. Precise visualization of the edge of the tumor is the key factor for removal of the whole tumor without damaging the healthy tissue that often leads to undesired postoperative consequences, e.g. impaired swallowing, articulation or damage of vocal folds.

Keywords: polymer carrier, RGD-based peptide, endoscopic surgery

Acknowledgements: This work was supported by Czech Science Foundation, grant 16-17207S and the Ministry of Health of the Czech Republic, grant 16-28594A.

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GALECTIN-3-TARGETED HPMA-COPOLYMERS BEARING GLYCAN LIGANDS

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In the present study we describe the synthesis and structure-activity relationship of conjugates of *N*-(2-hydroxypropyl) methacrylamide (HPMA) copolymers decorated with varying amounts of GalNAc β 1,4GlcNAc (LacdiNAc), a specific ligand of galectin-3 (Gal-3). Gal-3 is overexpressed in many cancer types and plays an important role in metastasis, tumorigenesis, tumour angiogenesis etc.¹ The synthetic water-soluble carriers based on HPMA copolymers represent an effective tool for site-specific targeting of drugs or other active agents *in vivo*.² The multivalent presentation of glycans enhances the affinity for the lectin biological target, and thus allows preferential accumulation of the conjugate at the desired site. First we synthesized polymer precursors by controlled radical Reversible Addition Fragmentation Chain Transfer (RAFT) polymerization. Then the glycans were conjugated to the statistic HPMA copolymers through diverse linkers (propargyl, dibenzocyclooctyne, ethynylphenyl and bivalent diethynylphenyl). Here, we present the synthesis, physico-chemical characterization and binding affinity of the prepared glycopolymers to Gal-3. The acquired data will help to develop advanced glycopolymers to target Gal-3 as a therapeutic goal in cancerogenesis and other disorders.

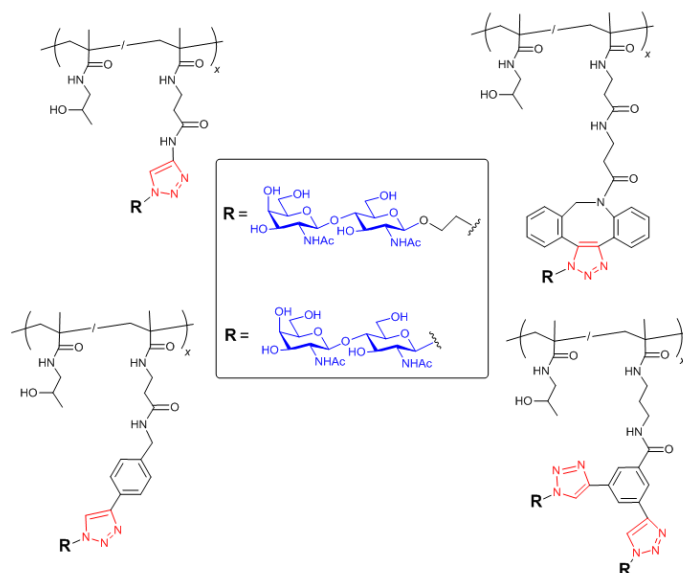


Figure 1. Conjugates of HPMA copolymers with functionalized saccharides conjugated through various linkers

References:

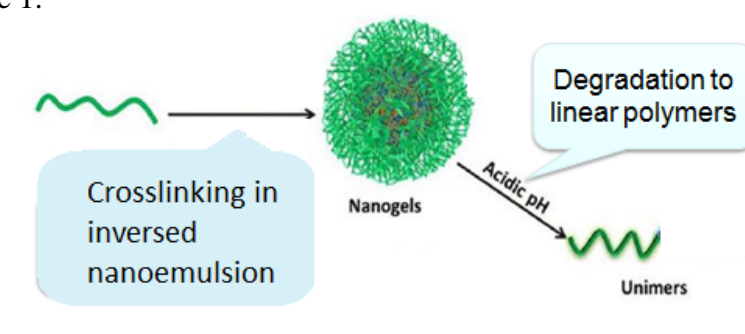
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NANO GEL BASED DRUG DELIVERY SYSTEM

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Polymer carriers based on *N*-(2-hydroxypropyl) methacrylamide (HPMA) copolymers and their drug conjugates represent very attractive nanotherapeutics, especially for neoplastic or inflammation diseases.¹ We focused on the synthesis of nanogel drug delivery systems based on HPMA designed for intravenous application serving as a long circulating depo. These carriers were synthesized with controlled radical polymerization technique (RAFT). Molecular weight of linear precursors was determined by size exclusion chromatography and content of hydrazide groups was determined spectrophotometrically. Nanogels were synthesized by crosslinking of the linear polymers through pH labile hydrazone bond. This bond is formed from hydrazide groups on the linear polymer and keto groups from crosslinking molecule (2,5-hexandione) and it is stable in a blood stream and degradable in the tumor environment. Linear copolymers were synthesized by a controlled copolymerization of HPMA and 1-(*tert*-butoxycarbonyl)-2-(6-methacrylamidohexanoyl)hydrazine in various molar ratios. Simplified scheme of the forming process and also expected degradation is shown on Scheme 1.



Scheme 1. Nanogel carrier synthesis and its degradation.

The size of nanogel was estimated with two methods: dynamic light scattering (DLS) and with nanoparticle tracking analysis (NTA). The estimated size of prepared nanogels was around 150 nm. Cytostatic drug doxorubicin was attached to the nanogel also via pH sensitive hydrazone bond.

Keywords: nanogel, nanoemulsion, HPMA, RAFT/

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BIODEGRADABLE TPS/PCL POLYMER SYSTEMS FOR MEDICAL APPLICATIONS

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Thermoplastic starch (TPS) and polycaprolactone (PCL) represent an interesting pair of biodegradable polymers for possible biomedical application with tailored properties. Starch is a cheap and natural abundant biodegradable polymer. However, it needs to be plasticized in order to be efficient in processing.^{1,2} TPS degrades very fast in comparison with other biodegradable polymers, but it has poor mechanical properties. Contrary to it, PCL degrades more slowly and it is ductile. The preferred polymers should be capable to create the polymer systems (TPS/PCL blends) with well-defined morphology-controlled drug release rate. The drug release is connected with TPS digestion and degradation, while the structural integrity is maintained due to PCL reinforcement. The morphology control of the polymer system during mixing and processing predominantly influences the mechanical properties, so detailed evaluation of the blend morphology is essential.³

In this work, we have studied the properties of TPS and TPS/PCL materials prepared from various types of starch (wheat, corn, and tapioca; Fig.1). We observed the morphology and measured the rheological and thermomechanical properties of pure TPS as well as TPS/PCL blends.

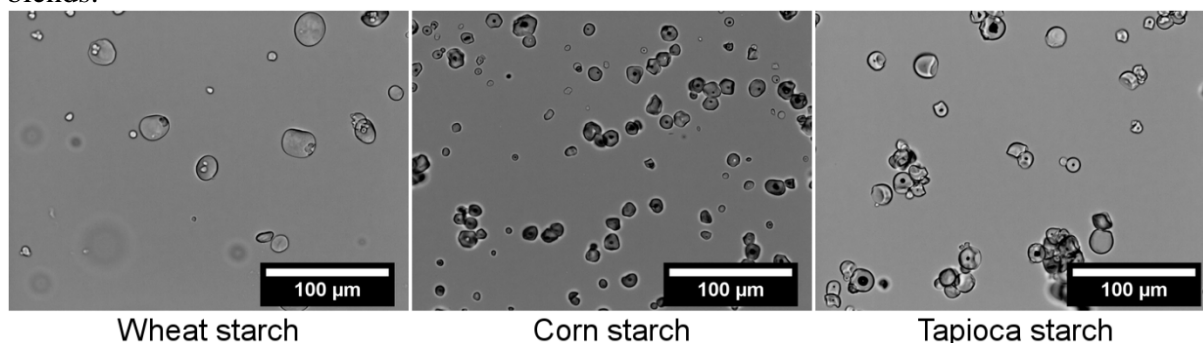


Figure 1. Light microscopy micrographs of native wheat, tapioca and corn starch (unit 100 μ m).

The results confirmed that the type of starch influenced the rheological and mechanical properties of TPS matrix as well as TPS/PCL blends.

Keywords: thermoplastic starch, polycaprolactone, morphology, rheology.

Acknowledgements: TE01020118 (TA CR), NV15-31269A (MZ CR), POLYMAT LO1507 (MSMT, NPU I).

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NANOSTRUCTURED SURFACES FOR BIOMEDICAL APPLICATIONS

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Human pluripotent stem cells (hPSC) are intensively studied due to their capacity to differentiate into all kinds of cells in the human body thus providing a universal source of therapeutic cells for regenerative medicine. Successful multiplication and differentiation of hPSC *in vitro* requires special substrates that provide the cells with integrin binding ligands mimicking those of native extracellular matrix.

We prepared new synthetic substrates for hPSC cell cultures consisting of a thin hydrophilic coating of poly(2-hydroxyethyl methacrylate-*co*-propargyl methacrylate) (82:18 mol%) and a bone sialoprotein-derived RGDT-peptide ligand that was covalently bound to the coating through the copolymer alkyne side groups. The advantage of this surface coating is that it can be prepared by a simple spin-or solution casting processes on polystyrene tissue culture substrates. We demonstrated that the coating is sufficiently stable in aqueous environment and effectively supports adhesion and proliferation of human embryonic stem cells (hESCs). We further investigated the effect of ligand surface concentration on hESCs behaviour and also characterized interaction of the coating with proteins contained in the cell culture media.

Localization of the peptide ligands into nanoclusters may enhance the signal effect of the ligands. To this end we attempted to bind the peptide to the poly(glycidyl methacrylate) nanospheres and subsequently to immobilize these clusters to the HEMA-based coating.

Keywords: human pluripotent stem cells, cell adhesion, peptide ligand, protein adsorption.

Acknowledgement: This work was supported by the Czech Science Foundation (Grant No. 16-02702S).

ANTIBACTERIAL MAGNETIC NANOPARTICLES: DESIGN, SYNTHESIS AND BACTERICIDAL EFFECT

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Monodisperse superparamagnetic magnetite (Fe_3O_4) nanoparticles, 16 nm in size according to transmission electron microscopy, were prepared by thermal decomposition of Fe(III) oleate and stabilized with oleic acid (Figure 1 a). To achieve good colloidal stability in aqueous biological media, the particles were coated with a silica shell of different thickness using water-in-oil reverse microemulsion technique, involving hydrolysis and condensation of tetramethyl orthosilicate. Resulting $\text{Fe}_3\text{O}_4@\text{SiO}_2$ particles maintained monodispersity (Figure 1 b) and were modified with thiol groups by reaction with (3-mercaptopropyl) trimethoxysilane. The $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SH}$ nanoparticles containing 1.1 mmol SH/g (from elemental analysis) were then decorated with silver nanoclusters ($\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-Ag}$; Figure 1 c) formed from nuclei growing on $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-SH}$ upon addition of NaBH_4 reducing agent. Surface modifications of the particles were analyzed by Fourier-transform infrared, energy-dispersive X-ray, and X-ray photoelectron spectroscopies; content of Ag was determined by atomic absorption spectroscopy. Colloidal stability was monitored by dynamic light scattering and magnetic properties were investigated by vibrating sample magnetometry. The $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-Ag}$ nanoparticles incubated with *Staphylococcus aureus* exhibited a good antibacterial activity.

Keywords: Magnetic nanoparticles; silica shell; thiol-functionalization; antibacterial activity.

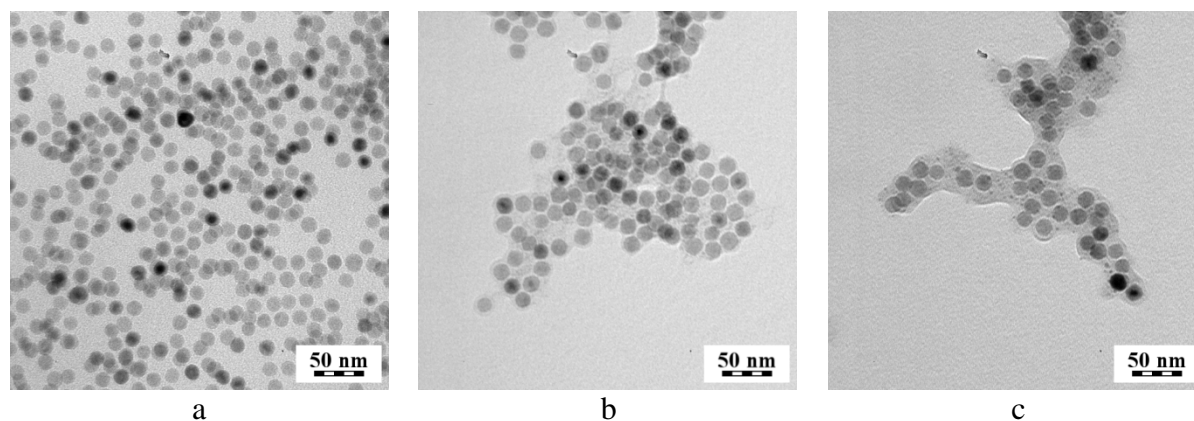


Figure 1. TEM micrographs of (a) Fe_3O_4 , (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2$, and (c) $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-Ag}$ nanoparticles.

Acknowledgement: Support of the Czech Science Foundation (No. 17-04918S) is acknowledged.

DESIGN AND SYTHESIS OF THIAZOLO[5,4-D]THIAZOLE OLIGOMERS FOR ORGANIC SEMICONDUCTORS

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The development of π -conjugated semiconductors for optoelectronic applications by alternating donor and acceptor units is the most common approach for the synthesis of low band gap materials. Thiazolo[5,4-d]thiazoles (TzTz), characterized by a rigid and coplanar structure, high stability and good electron acceptor properties are valuable starting materials for the design of electron accepting semiconductors. Additionally, thiophene derivatives have also been widely used as building blocks for optoelectronics because of their well-known stability as well as their tunable spectroscopic and electrochemical properties. The use of TzTz derivatives for various optoelectronic applications like OLEDs, OFETs, bulk heterojunction solar cells, emitters and fluorescent sensors, has been already demonstrated.¹⁻³ Following this concept, in this work our research focuses on synthesis and characterization of thiazolo[5,4-d]thiazole based π -conjugated molecules and polymers. Various substituted aromatic and heteroaromatic aldehydes and dithiooxamide were used as starting materials in various reaction conditions. Subsequently various π -conjugated systems were prepared by Suzuki coupling reaction. According to their optical and electrochemical properties, their applications in optoelectronics will be demonstrated.

Keywords: thiazolo[5,4-d]thiazole, π -conjugated systems, organic semiconductors

Acknowledgement: This work was supported by the Slovak Grant Agencies VEGA through projects No. 2/0158/17; 2/0161/17 and 1/0534/16.

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A MEMRISTIVE BEHAVIOR OF π -CONJUGATED POLYMER MOLECULARLY DOPED WITH ORGANIC ACCEPTORS

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Electrical properties of thin films composed of a mixture of π -conjugated polymer working as a donor and low-molecular weight organic acceptors have been studied. The system based on a copolymer containing derivatives of diketopyrrolopyrrole (DPP) and thiophene repeat units with admixed molecularly dispersed perylene derivatives showed a memristive behavior. Both DPP and the low-molecular weight perylene were properly substituted with alkyl groups for achieving a good solubility, which allowed thin films preparation using spin-casting technique. The charge carriers injected from the electrode into the organic thin film formed a space charge built in the boundaries between DPP and perylene domains, which limited further charge injection due to electrostatic repulsion between individual charges resulting in hysteresis of the current-voltage (I-V) characteristics. The dependence of hysteresis in the current-voltage characteristics on annealing and different ratios of DPP and perylenes has been studied. The devices exhibited lower hysteresis but increased conductivity after annealing. It can be explained by the reduced interface area between the donor and acceptor domains but increased intermolecular π - π interactions supporting the charge transport. The bi-stable behavior of current voltage was found to be influenced by presence of traps formed by adsorbed oxygen and water molecules in organic films. Both space charges and traps played an important role in the hysteresis and switching behavior of organic electronic devices.

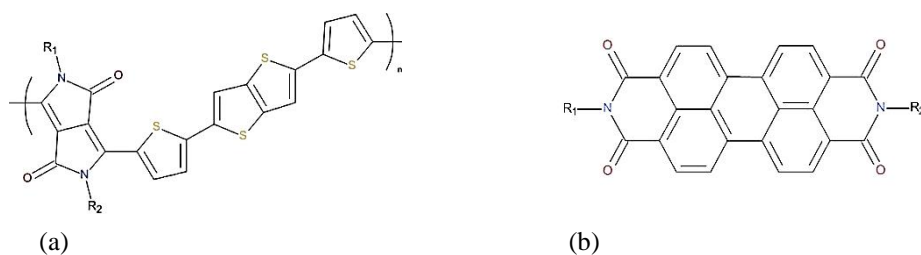


Figure 1. Chemical structure of (a) DPPDTT and (b) Perylene

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INFLUENCE OF DIP-COATING RATE ON PS-b-P4VP THIN FILMS PROPERTIES

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Block copolymer (BCP) thin films are widely investigated because of their ability to self-assemble into different morphologies, which makes them versatile substrates for applications in electronics, lithography, catalysis, photonics, biomedicine, photovoltaic devices, data storage or energy conversion.^{1,2} For most applications, it is important to control not only the desired BCP morphology, but also the thickness and roughness of obtained thin films. These parameters depend highly on the solvent properties and the film preparation technique. BCP thin films obtained via the dip-coating method have been proven to exhibit various morphologies depending on dip-coating rate.² That leads to a powerful method for producing different nanopatterns from a single BCP solution.

In this work the influence of dip-coating speed on the properties of polystyrene-*b*-poly(4-vinyl pyridine) (PS-*b*-P4VP) thin films was investigated. The films were prepared from 0.5 wt% 1-chloropentane solution of asymmetric PS-*b*-P4VP block copolymer, with $M_n(\text{PS}) = 124 \text{ kg/mol}$, $M_n(\text{P4VP}) = 12 \text{ kg/mol}$, and $M_w/M_n = 1.15$, with micellar structure and hydrodynamic radius $R_h = 46.55 \text{ nm}$, as measured by Dynamic Light Scattering and Small Angle X-Ray Scattering. Polymer films were deposited onto silicon wafers with withdrawal speed in the range 0.2-100 mm/min. The obtained thin films were characterized by the means of X-Ray Reflectivity, Atomic Force Microscopy and Grazing Incidence Small Angle Scattering. We report the influence of dip-coating rate on the obtained films' morphology, thickness and surface roughness. A V-shape dependence of film thickness vs withdrawal speed was obtained, which indicate that the chosen dip-coating rate range allowed to cover both the capillarity and draining regimes. The data were fitted using semi-empirical model, which allows to calculate the minimum film thickness $h_0 = 4.71 \text{ nm}$ obtained with critical dip-coating rate $u_c = 8.17 \text{ mm/min}$.³ It was found that when one regime of film formation (capillarity or draining) is dominant, the polymer films exhibit 'dot morphology' of P4VP blocks in a matrix of PS, with different sizes and center-to-center distances depending on the withdrawal speed. For intermediate speeds, where both mechanisms contribute in film formation, the morphology of closely packed spherical micelles with diameters about 45 nm was observed. These films also exhibited the highest RMS roughness (about 2.5 nm).

Keywords: PS-*b*-P4VP, block co-polymers, polymer thin films, self-assembly, dip-coating,

Acknowledgement: This work was supported by Internal Grant no 8604 of IMC AS CR v.v.i., Prague, Czech Republic

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**POLY(N-ISOPROPYLACRYLAMIDE), AND THE SYNTHESIS AND
THERMORESPONSIVE BEHAVIOR OF ITS
3-(TRIMETHOXYSILYL)PROPYL METHACRYLATE
BASED COPOLYMERS AND HYBRID GELS**

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One of the most intensively investigated class of smart materials belongs to poly(N-isopropylacrylamide) (PNIPAAm)¹ containing temperature responsive hybrid polymers, mainly because of their many application possibilities. The gel free synthesis of copolymers of NIPAAm and 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) up to relatively high TMSPMA contents, capable to undergo sol-gel reactions, was accomplished.² Due to the hydrophobic nature of TMSPMA, the cloud point (T_{CP}) and clearing point (T_{CL}) decrease with increasing TMSPMA content. Unprecedented hysteresis behavior of P(NIPAAm-co-TMSPMA) copolymers with higher TMSPMA contents were found, indicating catalyst free composition dependent gelation above the T_{CP} , i.e. under mild conditions.

Inorganic-organic hybrid gels of P(NIPAAm-co-TMSPMA) copolymers with high gel fractions by sol-gel processes were successfully prepared in both in the absence and presence of tetraethyl orthosilicate (TEOS). In contrast to the T_{CP} of copolymers, the thermal phase transition, i. e., the gel collapse temperature (GCT) of the resulting hybrid gels do not show significant composition dependence, it is in the range of 28-29 °C. Morphology investigations by SEM and SAXS indicate uniform distribution of the components without detectable large scale phase separation between the PNIPAAm and chemically connected silica components. Drug release experiments surprisingly show that these hybrid gels are able for sustainable release both under and above the GCT.³

Keywords: poly(N-isopropylacrylamide), 3-(trimethoxysilyl)propyl methacrylate, hybrid gel, drug release, sol-gel reaction

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ENVIRONMENTALLY RESPONSIVE BLOCK COPOLYMERS FOR INTRACELLULAR DELIVERY OF HYDROPHILIC THERAPEUTICS

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The extracellular and subcellular compartments are characterized by specific pH levels which can be considerably modified by pathophysiological states. Accordingly, when pH-stimuli responsive nano-assemblies are exposed to such milieus, they may respond by physicochemically changing their structure and/or surface charge.^{1,2} The structural changes of polymeric assemblies induced by environmental conditions can be exploited for the delivery of therapeutic drugs and genes into specific sites of action.³ In this framework, we highlight the potential use of pH-responsive block copolymers for the intracellular delivery of hydrophilic therapeutics. Several poly(*N*-(2-hydroxypropyl)methacrylamide)-*b*-poly[2-(diisopropylamino)ethyl methacrylate] diblock copolymers (PHPMA-*b*-PDPA) were synthesized by RAFT polymerization and characterized by NMR and SEC techniques. Self-assembled vesicular structures (polymersomes, PSomes) with a desirable size for cellular uptake ($R_H \sim 50$ nm) and low polydispersity (PDI = 0.07) were obtained from a selected block using microfluidics technique (MF) and characterized by static light scattering, zeta potential and confirmed by TEM micrographs (Fig. 1). Subsequently, the encapsulation and release of the chemotherapeutic drug doxorubicin and other potential therapeutic biomacromolecules will be investigated as well as the interaction of the produced PSomes with biologically relevant milieus.

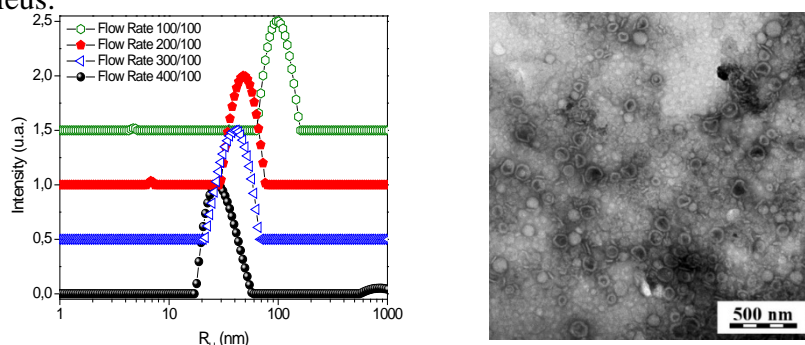


Figure 1. Size distribution for the produced PSomes by using MF in different flow rates (*left*) and TEM image of the PSomes produced from the PHPMA₃₅-*b*-PDPA₆₁ diblock copolymer in flow rate 200 $\mu\text{L}\cdot\text{min}^{-1}$ (PBS, pH 7.4)/100 $\mu\text{L}\cdot\text{min}^{-1}$ (polymer solution at 5 $\text{mg}\cdot\text{mL}^{-1}$).

Acknowledgement: The authors acknowledge the UNESCO/IUPAC Postgraduate Course in Polymer Science, the Czech Science Foundation (grant no. 17-09998S) and FAPESP (Grant 2017/11261-0).

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SMART AND SELF-HEALING PHOTSENSITIVE POLYMERS

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Smart polymers represent a new class of advanced materials. The stimuli responsive polymers respond to external stimuli, such as heat or light, by a change of physical properties. The self-healing polymers belong to the most promising applications of a smart behavior. They are stimuli responsive and possess the ability to self-heal when damaged. They are useful for many applications in biomedical and engineering fields.¹

Cinnamoyl, coumarin, anthracene, and azobenzene are the mostly used chromophore groups for photoresponsive systems by dimerization or isomerization reaction. As shown in Figure 1, using UV Lamp emitting at 365 nm we can cause creating dimers and in the result - network. UV crosslinking is reversible. By using UV lamp with wavelength 254 nm system can decrosslink.²

Based on the photosensitive commercial system - poly(vinyl cinnamate), the kinetics of the photo reaction was determined by IR measurement. To obtain materials with low T_g , series of polymethacrylate derivatives having cinnamoyl group in the side chain have been synthesized and the mechanical properties of the networks have been characterized.

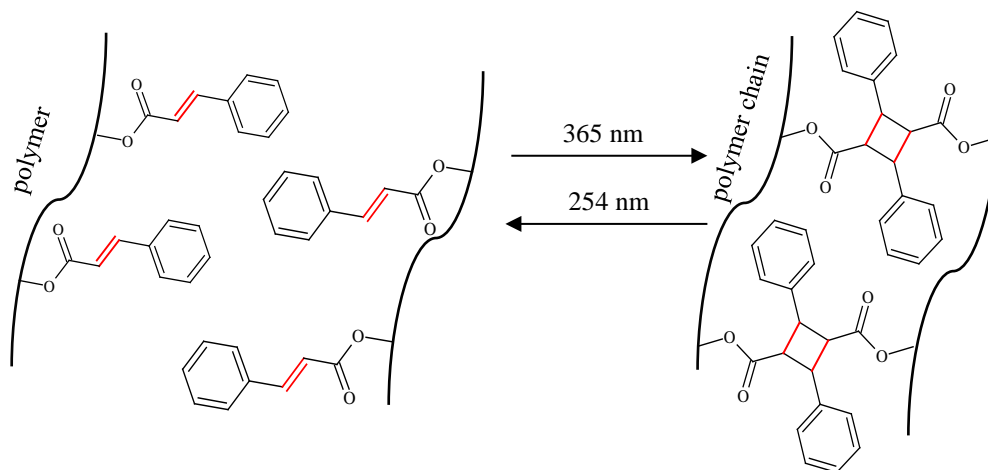


Figure 1. General mechanism of photocrosslinking.

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NOTES:

IMPACT OF THE HOFMEISTER SERIES ANIONS ON ETHYLENE GLYCOL BASED POLYMER BRUSHES

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Various studies have been focused on the impact of the Hofmeister series anions on the solubility of proteins, the aggregation behavior of block copolymers, the physicochemical properties of charged end-tethered polymer chains, etc. However, little attention has been given to investigation of the influence of the Hofmeister series on the structure, swelling behavior, viscosity and/or elastic modulus of ethylene glycol-based polymer brushes.

In this report we are focused on probing the responsive behavior of F^- , Cl^- and SCN^- anions on the physico-chemical properties of ethylene glycol-based polymer brushes using quartz crystal microbalance with dissipation monitoring (QCM-D). “Grafting from-“ approach was used to grow 2-hydroxyethyl methacrylate, oligo(ethylene glycol) methacrylate and oligo(ethylene glycol) methyl ether methacrylate polymer chains from surface-immobilized 2-bromo-2-methylpropanoyl groups using atom-transfer radical polymerization. The thickness and covalent structure of the brushes were probed utilizing spectroscopic ellipsometry (SE), grazing angle attenuated total reflection Fourier transform infrared spectroscopy (GAATR-FTIR) and X-ray photoelectron spectroscopy. *In situ* GAATR-FTIR and QCM-D revealed the changes in the molecular structure and viscoelastic properties of the brushes.

PHYSICAL-CHEMICAL PROPERTIES OF HYDRATED AND SELF-ASSEMBLED POLY(3,4-ETHYLENEDIOXYTHIOPHENE) CHAINS

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Poly(3,4-ethylenedioxythiophene) (PEDOT) has been attracting much attention as conducting polymer during the last decades because of its wide applications.¹ It was believed up to now that PEDOT structure and morphology does not changed during electrochemical performance, when over potential is not applied. Recently, we have shown that hydrated polymer chains are able to undergo re-arrangement during electrochemical testing.²

On **Figure 1a** the optical microscopy of PEDOT deposited on FTO electrode is presented. Under polarized light, the PEDOT does not show any anisotropic structure (**Figure 1b**). However, after electrochemical testing (particularly, repeating number of cyclic voltammetry) the PEDOT morphology changed to smooth film (**Figure 1c**) and under polarized light the formation of anisotropic structure is observed (**Figure 1d**). From our point of view such chains re-arrangements is possible only if they are well hydrated and not cross-linked. The presence of water in PEDOT was confirmed by using TGA and DSC measurements.²

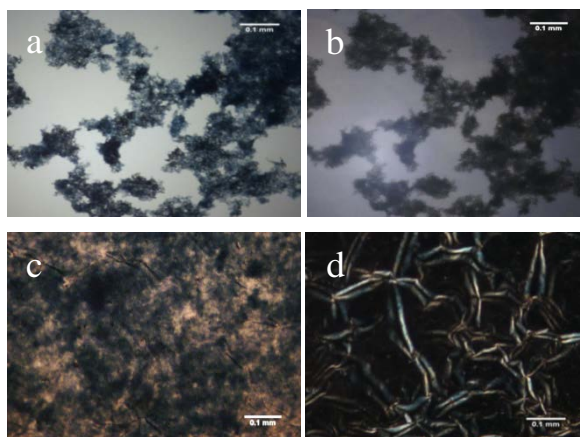


Figure 1. (a) Optical microscope of PEDOT film before and (c) after electrochemical measurements; (b) polarized optical microscope of PEDOT film before and (d) after electrochemical measurements.

We think that the knowledge about PEDOT chains re-arrangements during electrochemical performance is very important for PEDOT-based electro-device design.

Keywords: poly(3,4-ethylenedioxythiophene), electrochemical performance, chains re-arrangement.

Acknowledgement: We acknowledge Czech Grand Agency (grant number: 16-02787S).

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POLYHYDROXYALKANOATES (PHAS) OBTAINED FROM WASTE PLASTIC MATERIALS TO PRODUCE BIOPOLYMERS FOR NOVEL APPLICATIONS

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Alternatives to traditional petrochemical plastics are urgently required to reduce increasing levels of plastic pollution. Polyhydroxyalkanoates (PHAs) are a group of biocompatible, non-toxic and biodegradable plastics produced by bacteria that could be used as a synthetic plastic replacement.¹ The main factors limiting the widespread usage of PHAs are the high production costs and expensive chemical processing.^{1,2}

Oxidized polyethylene wax (O-PEW) and non-oxidized polyethylene wax (N-PEW) were used as carbon sources for PHA biosynthesis.^{1,2} The O-PEW was obtained from PE thermal degradation and N-PEW was formed using pyrolysis.^{1,2} These waxes were metabolized by *Cupriavidus necator* H16 in a bioreactor to produce PHAs. Fermentation was in both nitrogen rich and nitrogen-limited media. The biopolymers produced were analyzed using FTIR, NMR, GPC, TGA and electrospray ionization tandem mass spectrometry (ESI-MS/MS) to assess structure.^{1,2}

The accumulation of PHAs varied from 20 % to 40 % (wt/wt) of dry biomass in both growth media. When TSB was supplemented with O-PEW, bacteria produced PHA which contained 3-hydroxybutyrate and up to 3 mol % of 3-hydroxyvalerate and 3-hydroxyhexanoate co-monomeric units.² The ESI-MS/MS enabled PHA characterization when the content of 3-hydroxybutyrate was high and the appearance of other PHA repeating units was low.² When N-PEW was used, the PHA formed contained 3-hydroxybutyrate (HB) with 11 mol % of 3-hydroxyvalerate (HV) units.¹ MTT assays and SEM images demonstrated human HEK293 and WI-38 cells were successfully grown on 3D printed PHA-blend scaffolds for 7 days, with no signs of toxicity. In conclusion O-PEW and N-PEW could be a promising carbon source and the PHAs produced can be applied to novel medical applications.

Keywords: Polyhydroxyalkanoates, PHAs, bioplastics, wax, pollution

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EFFECT OF SAFRANIN ON THE POLYMERIZATION OF PYRROLE: MORPHOLOGY AND CONDUCTIVITY CONTROL

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Conducting polymers, especially polypyrrole (PPy), have received high attention due to their unique properties such as biocompatibility and tunable electrical conductivity, which can be controlled by reversible doping. The potential applications may concern sensors, supercapacitors, biomedical devices and adsorbents. Further improvement of PPy properties like increasing its conductivity, specific surface area and processability is still a primary goal. These properties are mainly dependent on the morphology, which can be tuned to one-dimensional by using templates like dyes.^{1,2}

PPy was synthesized by the oxidation of pyrrole with iron chloride in the presence of safranin, which works as structure guiding template. The effects of dye concentration, oxidant/monomer molar ratio and polymerization temperature on the morphology and electrical conductivity were studied. Prepared PPy was characterized by scanning and transmission electron microscopy, FTIR and Raman spectroscopies and conductivity measurement. Results showed that both morphology and conductivity were found to be affected by safranin concentration. SEM and TEM images confirmed the formation of well-defined nanofibers (Fig 1a). Conductivity measurements showed the highest values, 35 S cm⁻¹ in the case of 0.004 M safranin compared to 5 S cm⁻¹ for the globular PPy (Fig 1b).

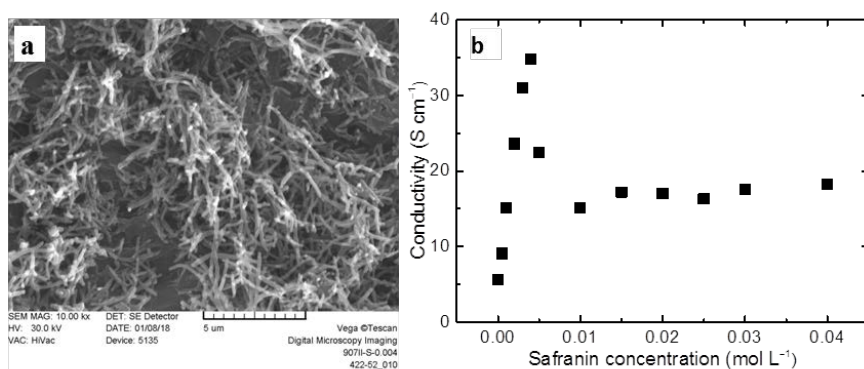


Figure 1. SEM micrograph of polypyrrole prepared in the presence of 0.004 M safranin (a) and the conductivity of polypyrrole prepared with different concentrations of safranin (b).

Keywords: Conducting polymer; Polypyrrole; Safranin; Nanofibers; Conductivity.

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THREE-DIMENSIONAL CARBON-BASED POLYMER SCAFFOLD FOR BONE TISSUE ENGINEERING

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Bone tissue engineering is devoted to the development of biocompatible materials suitable for the replacement of defect bone tissue.¹ Bones represent a very dynamic structure and its understanding is the basis for designing materials mimicking the extracellular matrix.² A porous 3D carbon based material was produced by thermal modification of polyacrylonitrile at 360°C with air access. Morphological structure is created by interconnected pores that were characterized by scanning electron microscope. Communicating pores of sizes suitable for the growth and proliferation of human osteoblasts were formed in the structure by incorporation and subsequent washing of the porogen particles - fractionate crystals of sodium chloride. The mechanical properties of the material were improved by introduction of a secondary interpenetrating chitosan network. Proposed material and its hydroxyapatite composite have been studied in biological experiments for their osteoconductivity. The materials proved to be non-cytotoxic and their chemical composition and morphological structure promote the adhesion, proliferation and growth of human osteosarcoma cell line MG 63 strain that formed a confluent layer on the scaffolds.

Keywords: polyacrylonitrile, bone tissue engineering, chitosan, scaffold.

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APPLICATION OF ZEOLITES IN FISH BREEDING AND THEIR EFFECT ON NITRIFYING MICROORGANISMS

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This research is focused on the sustainability of water in fish breeding, in terms of the content of ammonium ions produced by fish metabolism. The self-production of ammonium ions is unfavourable for the fish stock in the tanks and requires frequent water change in the tanks. The aim of the project is to minimize the concentration of ammonium ions in water by the application of zeolite filters, thereby reducing the operating costs mainly due to lower water consumption.

During the experiments, the interaction between zeolite sorbents and the nitrifying bacteria was monitored. The water pollution is slowed down by a competition between zeolites and the nitrifying bacteria for present ammonium cations.¹

Three zeolite materials (KlinoMn, BBC and geopolymeric zeolite A) were tested in terms of their ammonium cations (NH₄⁺) exchange kinetics. In the next phase of testing, these materials were installed into two-chamber filters which were placed in the aquaria. The results were compared with the other aquaria systems where the same two-chamber filters with foam filling were used which served as a carrier for nitrifying bacteria. The most effective zeolite material was chosen for operational conditions in culture tank breeding of koi carp (*Cyprinus carpio haematopterus*).

Nitrifying bacteria present in the foam carriers were identified by the molecular biology method FISH (fluorescence *in situ* hybridization). Bacteria of both nitrification stages were determined. Representatives of the AOB (ammonia oxidizing bacteria) – bacteria of the genus *Nitrosomonas* were found in small amounts while the NOB (nitrite oxidizing bacteria) were present in a large quantity, represented by the genus *Nitrospira*.

None of the zeolite materials negatively influenced the fish life. Of all tested materials, the non-synthetic KlinoMn was the most suitable as it maintained the pH value of water in the optimal range of 7.5–7.9. A positive effect of zeolite materials was confirmed in the operating conditions.

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