macro PRAGUE

Akademie věd České republiky

Strategie AV21

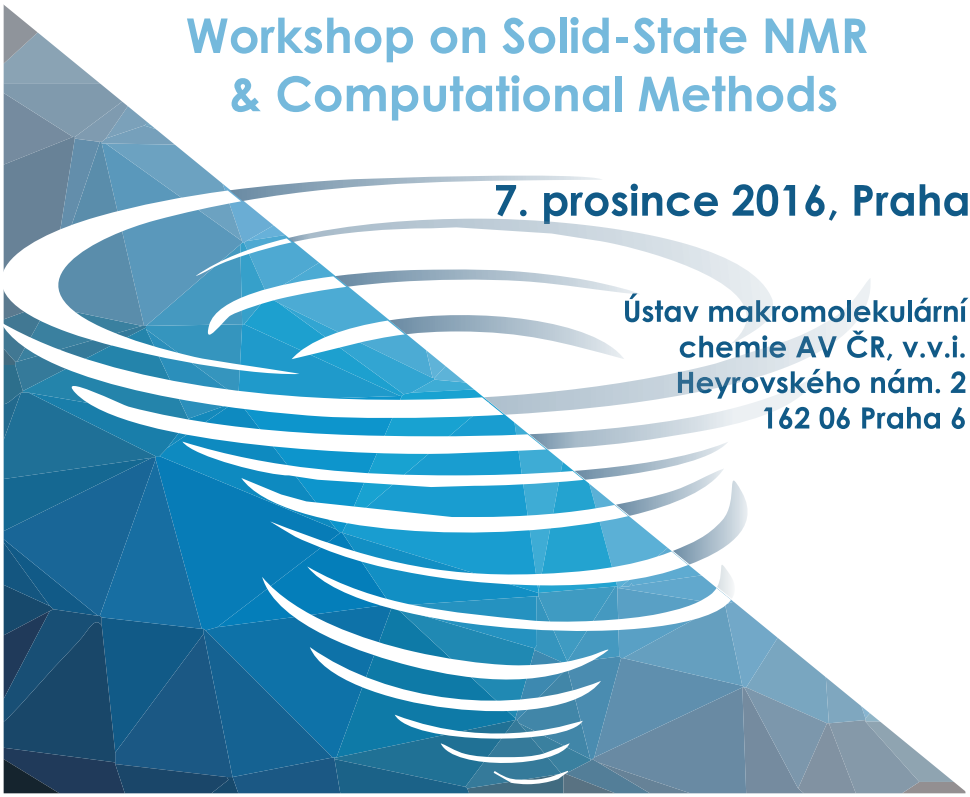
Špičkový výzkum ve veřejném zájmu

10. WSSNMR

Workshop on Solid-State NMR & Computational Methods

7. prosince 2016, Praha

Ústav makromolekulární chemie AV ČR, v.v.i.
Heyrovského nám. 2
162 06 Praha 6



Společná laboratoř NMR spektroskopie pevného stavu
ÚMCH AV ČR, v.v.i. a ÚFCH JH AV ČR, v.v.i.

pořádají

dne 7.12.2016

v

klubu B a C
Ústavu makromolekulární chemie AV ČR, v.v.i.
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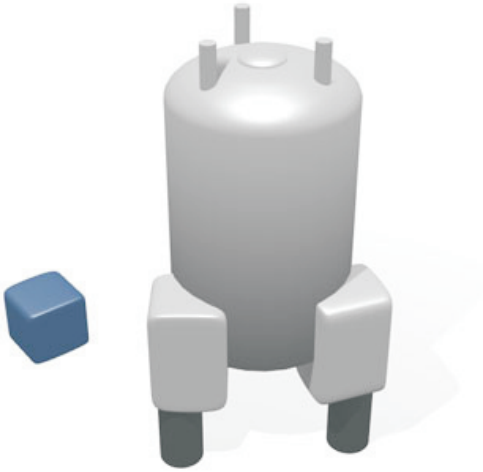
10.workshop NMR pevného stavu a souvisejících výpočtových metod



S·S NMR
IMC AS CR & JHI AS CR

NMR krystalografie jako spojnice mezi základním a průmyslovým výzkumem, Strategie AV21

Program

8:55	*Zahájení*
9:00 - 9:20	**Czernek Jiří** *UMCH AV ČR_* Computational Investigations into Structural and NMR-Spectroscopical Parameters of Active Pharmaceutical Ingredients
9:20 - 9:35	**Kukačková Olívia** *UMCH AV ČR_* Solid-state NMR study of i-PP interface
9:35 - 9:50	**Konefał Rafal** *UMCH AV ČR_* Thermoresponsive polyoxazoline homopolymers and copolymers aqueous solutions studied by NMR spectroscopy
9:50 - 10:10	*přestávka na kávu*
10:10 - 10:30	**Spěváček Jiří** *UMCH AV ČR_* Thermoresponsive block copolymers in aqueous medium studied by NMR and other methods
10:30 - 10:50	**Kratochvíl Bohumil** *VŠCHT_* Jev polymorfismu v přírodě
10:50 - 11:10	**Abbrent-Nováková Sabina** *UMCH AV ČR_* Effect of polymer network structure on physical and chemical properties of resulting gel polymer electrolyte materials
11:10 - 11:30	**Kobera Libor** *UMCH AV ČR_* Spying On Fe-Ions And Their Role In Modified Aluminosilicates During Sorption Of Anions Using ssNMR Spectroscopy
11:30 - 13:00	*přestávka na kávu a oběd*
13:00 - 13:20	**Stepan Sklenak** *ÚFCH JH AV ČR_* DFT calculations of NMR parameters of framework Al atoms and extra-framework monovalent cations in silicon-rich zeolites
13:20 - 13:40	**Dědeček Jiří** *ÚFCH JH AV ČR_* Stability of framework structures of *BEA zeolite Multinuclear MAS NMR and ab initio study
13:40 - 14:00	**Urbanová Martina** *UMCH AV ČR_* Alginate beads cross-linked by different ions as seen by Solid-state NMR
14:00 - 14:20	**Vetchý David** *VFU, Brno_* Mukoadhezivní orální filmy
14:20 - 14:40	**Gajdziok Jan** *VFU, Brno_* Liquisolid systems as modern drug formulations
14:40 - 15:00	*přestávka na kávu*
15:00 - 15:20	**Brus Jiří** *UMCH AV ČR_* NMR crystallography of hybrid MIL53(Al)–[LiCo-bis-dicarbollide] MOF for Li-batteries
15:20 - 15:40	**Jegorov Alexandr** *TEVA_* Strukturní analýza v registrační dokumentaci API včera, dnes a zítra
15:40 - 16:00	**Veverka Václav a Vrzal Lukáš** *ÚOCHB AV ČR_* Combining Ligand And Protein Perspectives In Fragment-Based Drug Discovery
16:00 - 16:20	**Kratochvíl Bohumil** *VŠCHT_* Žebříčky (rankings) univerzit
16:20	*Zakončení - diskuse k projektu*
16:30 - 21:59	*neformální diskuse*

Abstrakta

Computational Investigations into Structural and NMR-Spectroscopical Parameters of Active Pharmaceutical Ingredients

Jiří Czernek*, Jiří Brus

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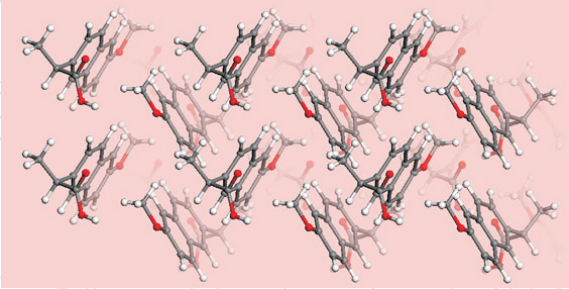
In pre-dossier studies, the chemical information about an active pharmaceutical ingredient (API) needs to be collected and analyzed. The knowledge of structural forms of an API in the solid state may become indispensable, and the related experimental studies most frequently employ the techniques of the X-ray diffraction (XRD) and the solid-state nuclear magnetic resonance (SSNMR) spectroscopies. Important insights into the XRD and SSNMR data for APIs can be provided by the density-functional theory (DFT) based calculations, especially if performed in the pseudopotential plane-waves scheme with the periodic boundary conditions imposed, thus treating the investigated solid-phase structure as an infinite system (see the model of naproxen shown below). Here the recent developments in this area will be presented, with the focus on

O the description of the SSNMR-consistent crystal structures [1]; this will be illustrated by the comparison of the XRD and DFT geometries of **vitamin B1** hydrochloride and of its monohydrate, which have been described with the inclusion of the 13-C and 15-N SSNMR parameters; and

O the theoretical prediction of the two-dimensional SSNMR spectra [2], [3]; the underlying statistical treatment of the level of agreement between the DFT calculations (performed for either known or tentative structures) and measurements will be discussed, with **metergoline** [2], **naproxen** [4] and **decitabine** [5] taken as examples.

[1] J. Czernek, T. Pawlak, M. J. Potrzebowski, J. Brus, *Chem. Phys. Lett.* **2013,** *555*, 135–140. DOI:10.1016/j.cplett.2012.11.002
[2] J. Czernek, J. Brus, *Chem. Phys. Lett.* **2013,** *586*, 56–60. DOI:10.1016/j.cplett.2013.09.015
[3] J. Czernek, J. Brus, *Chem. Phys. Lett.* **2014,** *608*, 334–339. DOI:10.1016/j.cplett.2014.05.099
[4] J. Czernek, *Chem. Phys. Lett.* **2015,** *619*, 230–235. DOI:10.1016/j.cplett.2014.11.031
[5] J. Brus, J. Czernek, L. Kobera, M. Urbanová, S. Abbrent, M. Hušák, *Cryst. Growth Des.* **2016**



Abstrakta

Multivariabilná analýza ss-NMR parametrov polypropylén–uhličitan vápenatých nanokompozitov s rôznou húževnatosťou

Olívia Kukačková

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V tomto projekte sme sa zamerali na pochopenie vzájomných súvislostí medzi mechanickými vlastnosťami a ss-NMR parametrami skúmaných vzoriek na molekulárnej úrovni.

Na základe tohto kontextu boli študované a analyzované odlišnosti medzi vzorkami polypropylén-uhličitan vápenatých nanokompozitov s troma rôznymi typmi modifikácií v systéme: *a)* pomer polypropylen (PP)-plnivo – 80/20 a 60/40; *b)* dve veľkosti častíc plniva – 1.7 µm (1VA) a 12 µm (15VA); *c)* dva typy ošetrenia plniva pomocou mastnej kyseliny – kyseliny olejovej (OA) alebo stearovej (SA); a tiež systémy bez ošetrenia mastnej kyseliny. Celkovo bolo analyzovaných trinásť variant PP materiálu s odlišnými mechanickými vlastnosťami a veľmi jemnými štruktúrnymi odlišnosťami. Vzorky boli podrobené analýze húževnatosti a spektrálne analyzované pomocou základných ^{13}C CP/MAS a ^{13}C MAS NMR experimentov s variabilnou teplotou (VT) od 296K do 355K. Výsledné ss-NMR dáta boli spracované pomocou multivariabilnej analýzy.

Toto použitie ssNMR spektroskopie v kombinácii s faktorovou analýzou nám ponúklo využitie základných a ťažko rozlíšiteľných ssNMR dát k zisteniu jemných spektrálnych odlišností medzi vzorkami s rôznymi štruktúrnymi modifikáciami a mechanickými vlastnosťami.

Abstrakta

Thermoresponsive block copolymers in aqueous medium studied by NMR and other methods

Jiří Spěváček, Rafał Konefał, Jiří Dybal, Jana Kovářová

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It is well known that poly(*N*-isopropylacrylamide) (PNIPAm) and other thermoresponsive polymers show in aqueous solutions a lower critical solution temperature (LCST). They are soluble at lower temperatures but heating above the LCST results in phase separation which makes solutions milk-white turbid. On the molecular level, both phase separation in solutions and similar volume phase transition in hydrogels are assumed to be a macroscopic manifestation of a coil-globule transition followed by further aggregation. Their thermosensitivity makes these polymer systems interesting for miscellaneous biomedical and technological applications.

Using NMR combined with FTIR spectroscopy and DSC we studied D_2O solutions of block copolymers poly(ethylene oxide) (PEO)-PNIPAm; these copolymers are soluble in water at room temperature but at elevated temperatures they form micelles [1]. Both linear diblock PEO-*b*-PNIPAm and Y-shape triblock PEO-*b*-$(PNIPAm)_2$ copolymers with various length of PNIPAm block were studied. Formation of micellar structures results in a marked broadening of ^{1}H NMR signals for a major part of PNIPAm segments. The fraction of PNIPAm units with significantly reduced mobility (units in micellar core) then can be determined from reduced integrated intensities in high-resolution NMR spectra [2]. To obtain information on the behaviour of water (HDO) molecules we used measurements of spin-spin relaxation time T_2. We have found that presence of the PEO block and copolymer architecture significantly affect phase transition and structures of PNIPAm component, as well as behaviour of water molecules. From ATR FTIR spectra combined with quantum-chemical calculations it follows that at temperatures above the transition the degree of dehydration of PNIPAm segments (C=O groups) is higher in block copolymers in comparison with suspension of the neat PNIPAm. For PEO-PNIPAm diblock copolymer 2D ^{1}H-^{1}H NOESY NMR spectra revealed certain conformation changes already in the pre-transition region.

Acknowledgment: Support by the Czech Science Foundation (project 15-13853S) is gratefully acknowledged.

[1] W. Zhang, L. Shi, K. Wu, Y. An, *Macromolecules* **2005**, 38, 5743-5747.
[2] J. Spěváček, *Curr. Opin. Colloid Interface Sci.* **2009**, 14, 184-191.

Abstrakta

Effect of polymer network structure on physical and chemical properties of resulting gel polymer electrolyte materials

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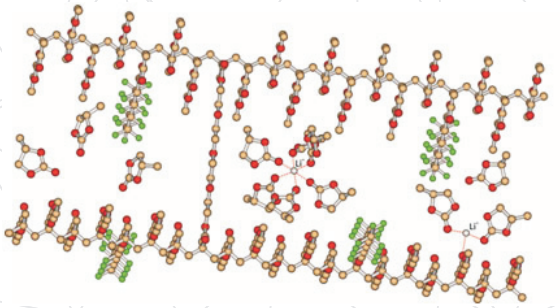
Gel polymer electrolytes (GPE) based on 2-ethoxyethyl methacrylate with various amounts of fluorine-containing co-monomer, 2-(perfluorooctyl) ethyl methacrylate (F17EMA), were prepared, with 1M $LiClO_4$ in propylene carbonate as solvent and crosslinked with n-ethylene glycol dimethacrylate monomers where n is in the range from one to four. It was shown that ionic conductivity and mechanical properties were greatly dependent on both the amount of solvent and salt used, but also on the combined impact from the content of fluorinated monomer and the type of cross-linker. The best results within our experimental series were achieved with the GPE containing the longest cross-linker (tetraethylene glycol dimethacrylate) and 10 wt% of the fluorinated co-monomer. [1]

In the current study we put forward a working hypothesis to explain these results by thoroughly examining the network structure of the UV-polymerised gels. We assessed the impact of the used components concentrations on the cross-link density (concentration of elastically active network chains). [2] The cross-link density was determined from equilibrium swelling and equilibrium modulus of elasticity of the swollen samples in the linear viscoelasticity region of the networks. Also the flexibility of the system as a function of dilution at network preparation was established. Finally, chain composition and sequencing of the co-monomers were investigated.

References

[1] J. Michálek, S. Abbrent, M. Musil, J. Kovářová, J. Hodan, J. Dybal, *Electrochim. Acta*. **208** (2016) 211- 224, doi:10.1016/j.electacta.2016.05.057.

[2] M. Dušková-Smrčková, H. Valentová, A. Ďuračková, K. Dušek, Effect of Dilution on Structure and Properties of Polyurethane Networks. Pregel and Postgel Cyclization and Phase Separation, Macromolecules. 43 (2010) 6450–6462. doi:10.1021/ma100626d



Abstrakta

Alginate beads cross-linked by different ions as seen by Solid-state NMR

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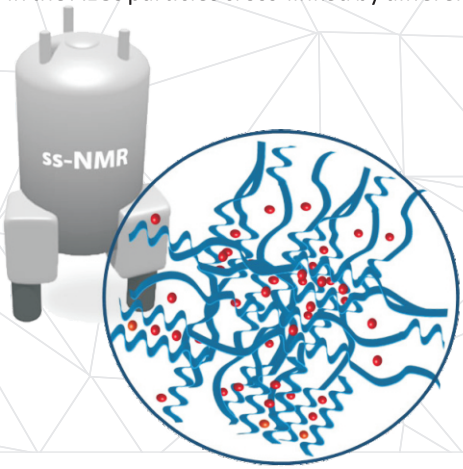
Alginates (ALGs) are linear unbranched polysaccharides, which consist of two basic building units; α-L-guluronic acid (G) and β-D-mannuronic acid (M) residues linked by glycosidic bonds, forming homopolymeric and heteropolymeric blocks. They are widely used in pharmacy and currently they are extensively investigated for many biomedical applications (including wound healing, drug delivery and tissue engineering applications) due to its biocompatibility, non-toxicity, non-immunogenicity, biodegradability and relatively low cost. The main advantages of ALGs beads are the ability to control release of encapsulated materials, protection of the encapsulated materials against degradative reactions in the external environment, masking the organoleptic properties such as color, taste and odour of encapsulated materials etc. All these properties and applications are ultimately dependent on molecular architecture and gelling mechanism.

In our work different ions (Al^{3+}, Zn^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}) cross-linked alginate beads were prepared through external ionic gelation. Our aim was to find influence of different cross-linking ions, such as calcium (II), zinc (II), aluminium (III), manganese (II), strontium (II) or barium (II), on resulting structure of the prepared alginate (ALG) beads. All the prepared systems were detailed structure characterized by a range of solid-state NMR techniques. In detail we discussed of basic 1H; 1H MAS; ^{23}Na MAS and ^{13}C CP/MAS NMR experiments. The influence of different ions on resulting segmental motions of prepared ALG microparticles was obtained by 2D ^{1}H-^{13}C SLF-PILGRIM NMR experiments. The application of the ^{23}Na-^{23}Na DQ (double-quantum) experimentation opened a new way for understanding the structural role of residual Na^{+} ions in the ALGs particles cross-linked by different ions.



Abstrakta

Mukoadhezivní filmy pro terapii defektů ústní dutiny

David Vetchý

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Problém terapie defektů ústní dutiny spočívá v aplikační formě. Zatímco na kůži je možno aplikovat různé formy krémů, mastí, nebo gelů, které zůstávají na povrchu relativně dlouho, v dutině ústní je jejich aplikace obtížná a preparáty se na sliznici neudrží po dostatečné dlouhou dobu. Důvodem je vlhké prostředí v dutině ústní, téměř permanentní pohyb jazyka a tvářové sliznice, a trvalé omývání sliznice slinou. Relativní nevýhodou rovněž zůstává často nepříjemná chuť preparátu a u některých obsah alkoholu. Překonat zmíněné problémy lze novou lékovou formou – mukoadhezivními orálními filmy. Díky jejich vlastnostem dojde k přilnutí na povrch sliznice, tzv. mukoadhezi. Mohou tak krýt postižená místa a prodlužovat účinek lokálně působících léčiv. Mukoadhezivní filmy nabízí i řadu dalších výhod oproti jiným lékovým formám díky svému tvaru, velikosti a tvarové flexibilitě (minimalizují omezení při mluvení, příjmu potravy, tekutin a pocitu cizího tělesa v ústech) [1]. Pro přípravu mukoadhezivních filmů se používá široká škála filmotvorných polymerů. Rozdílnosti mezi monomery mají vliv na rozpustnost, flexibilitu nebo pevnost připravených filmů. Mezi základní charakteristické vlastnosti vhodných filmotvorných polymerů patří jejich hydrofilita, visko-elasticita, schopnost řetězců polymeru rychle penetrovat do hlenové vrstvy pokrývající sliznici dutiny ústní a velký počet polárních skupin tvořících s mucinem v dutině ústní vodíkové můstky. Zásadními pomocnými látkami pro přípravu mukoadhezivních filmů jsou plastifikátory, které ovlivňují flexibilitu a redukují křehkost připraveného filmu. Nejčastěji užívanými plastifikátory jsou glycerol, propylenglykol, polyethylenglykoly s nízkou molekulovou hmotností, sebakáty, citráty a ricinový olej. Nejrozšířenější technikou přípravy mukoadhezivních filmů je tzv. metoda odpařování rozpouštědla. Filmotvorné polymery, plastifikátor, léčivo a případné další pomocné látky se rozpouštějí nebo dispergují ve vhodných rozpouštědlech a následně se vzniklé homogenní směsi dávkují do odlévacích forem. Poté se rozpouštědlo odpařuje za pokojové nebo zvýšené teploty. Finálním krokem je úprava filmu do požadovaného tvaru a velikosti.

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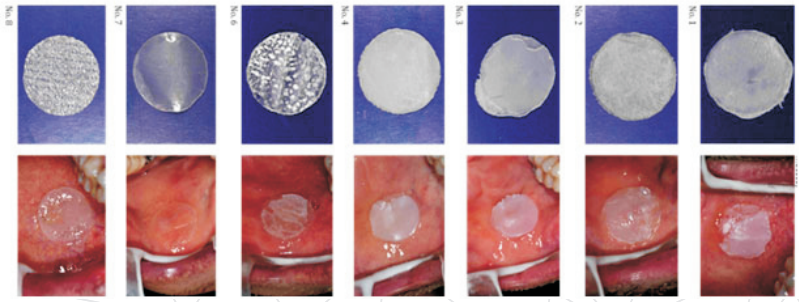

Abstrakta

Liquisolid systems as modern drug formulations

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It is estimated that up to 40% of drugs commonly used in current pharmacotherapy show poor water solubility. Their low dissolution rate in gastrointestinal fluids often negatively influences the rate and extent of drug absorption into the systemic circulation after oral administration. Therefore, scientific literature describes several techniques used to enhance the dissolution rate and the absorption efficiency and bioavailability of water limited-soluble (atorvastatin, carbamazepine, diclofenac, furosemide, etc.) and/or liquid lipophilic drugs (tocopherol acetate, clofibrate, etc.). One of the most promising and innovative technique for promoting dissolution and in vivo bioavailability of poorly soluble drugs is the formulation of liquisolid systems (LSS) [1].

LSS could be described as powdered forms of drug in liquid state. Drug in liquid state can be transformed into the dry-looking, non-adherent, free flowing and readily compressible powder by simple blending with excipients with high adsorption capacity called carriers. These materials show capability to incorporate liquid into its porous structure. Second essential excipients used during LSS formulation are coating materials that adsorb liquid layer formed on the saturated carrier particle surface and improve flowability of the powder blend. The drug in liquid state could be applied on the particles of the carrier by spraying in fluid bed equipment or by stirring in high-shear mixers to ensure good homogeneity of the prepared liquisolid blend. The prepared obtained dry blends can be subsequently transformed into conventional solid dosage forms (e.g. filled into capsules or compressed into tablets) [2].

LSS show many advantages in comparison to other dosage forms influencing drug bioavailability, e.g. lower production costs, similar final processing as tablets or hard capsules, minimized pH influence on dissolution rate and possibility to prepare dosage forms with controlled drug delivery. The main benefit of LSS represents their enhanced in vitro dissolution rate and hence improved in vivo bioavailability of poorly soluble drugs, which are presented in the dissolved state and thus are directly available for absorption in GIT. Moreover, the presence of the non-volatile solvent facilitates the wetting of the drug particles by decreasing the interfacial tension between dissolution medium and dosage form surface. Therefore, many poorly soluble drugs (such as atorvastatin, carbamazepine, furosemide, indomethacin, etc.) have been formulated as liquisolid systems to ensure enhanced drug release and improved bioavailability of the active ingredient [3].

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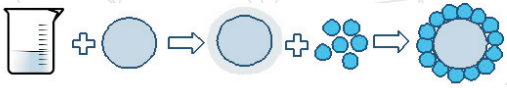
[2] B. Vraníková, J. Gajdziok, D. Vetchy, *BioMed Research International* **2015** DOI: http://dx.doi.org/10.1155/2015/608435.
[3] B. Vraníková, J. Gajdziok, *Acta Poloniae Pharmaceutica - Drug Research* **2015**



Abstrakta

Efficient and easy-to-implement solid-state NMR strategy for mapping the architecture of *liquisolid* mesoporous silica drug-delivery devices

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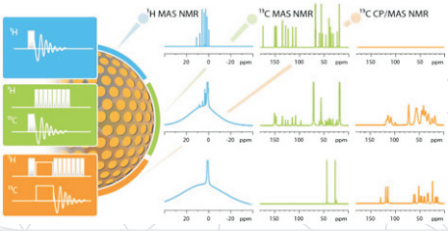
An increasing number of currently discovered compounds with desirable biological activity may never reveal their true potential because of unfavourable physicochemical properties of the bulk material. Particularly, for poorly water-soluble drugs which comprise ca. 40% of the new chemical entities currently being discovered, oral administration in solid dosage forms is problematic because it may pose a risk of compromised bioavailability. Recent effort in optimizing therapeutic efficacy, however, has resulted in the development of novel biocompatible and optionally stimuli-responsive drug-delivery devices, liquisolid systems (LSS), which combine advantages of pharmaceutical solids and liquids, such as comfort of oral administration and the efficient absorption from the gastrointestinal tract, respectively.

In this contribution we have focused on the development of a reliable, robust and easy-to-implement strategy for monitoring the structure and assembly of organic compounds in variable liquid/solid environments of MSNs. The proposed strategy allowing to probe arrangement and physical state of active compounds incorporated on the surface of mesoporous silica particles is surprisingly simple and based on the combination of three most straightforward solid-state NMR techniques: *i*) ^{1}H MAS NMR, *ii*) T_1-filtered ^{13}C MAS NMR, and *iii*) ^{13}C CP/MAS NMR experiment (Figure 1). Each of the applied experiments provides specific, mutually complementing, data that reflect molecular arrangement and dynamic processes occurring at different motional regimes. In combination, these experimental data serve as ideal basis to reconstruct a surprisingly comprehensive picture of the internal architecture of *liquisolid* systems.

Schematic representation of the applied ss-NMR experiments (^{1}H MAS NMR (blue); ^{13}C MAS NMR (green); and ^{13}C CP/MAS NMR (orange)) and the corresponding spectra of different types of liquisolid systems.



Abstrakta

Jev polymorfismu v přírodě

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Polymorfismus byl původně definován jako tvarová rozmanitost krystalů jedné chemické entity v závislosti na podmínkách krystalizace. V důsledku rozvoje RTG difrakčně-strukturních metod byla definice polymorfismu zpřesněna tak, že polymorfy jedné chemické entity se musí lišit svojí krystalovou strukturou, z které plynou i jejich rozdílné fyzikálně-chemické vlastnosti. Pro tvarovou rozmanitost krystalů, beze změny krystalové struktury, byl vymezen pojem krystalového habitu (designu, morfologie). V současnosti má největší význam polymorfismus farmaceutických substancí. Také zde lze pozorovat určitý vývoj, který byl odstartován objevem dvou polymorfů ranitidinu hydrochloridu, které vyvolaly soudní spor (1978-1995). Posléze se světově známou stala i kauza "disappearing polymorph" ritonaviru, inhibitoru HIV-proteasy (1996-2000). S příchodem nového tisíciletí se s polymorfy ve farmacii doslova roztrhl pytel a začaly být publikovány a patentovány i polymorfy, které mají pouze teoretický význam (např. polymorph II aspirinu, 2005). Dnes si žádná farmaceutická firma nedovolí ignorovat polymorfismus svých substancí a jsou široce vyvíjeny metody polymorfního "screeningu" a predikce. Z tohoto důvodu lze v současnosti pozorovat i určitý odklon a přehodnocení jevu polymorfismu národními regulačními institucemi. Paradoxně na úkor polymorfismu nabývá na významu řízený design a distribuce velikostí částic farmaceutických substancí jako klíčového parametru pro pokročilé farmaceutické formulace.

Abstrakta

Žebříčky (rankings) univerzit

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Od roku 2003 jsou univerzity podle výkonnosti a prestiže řazeny do žebříčků (rankings). Samozřejmě, že pro tvůrce těchto žebříčků je to především dobrý a rostoucí byznys. Některé státy od pozice univerzity v žebříčku totiž začínají odvozovat její finanční dotaci. Kvalifikovaný odhad tvrdí, že na světě je více než 26 000 univerzit a žebříčků je na trhu asi 30. Některé jsou globální, některé regionální, každý má jinou hodnotící metodiku, takže pozice jedné univerzity se liší od žebříčku k žebříčku. Postupem času si největší prestiž si vydobyly tři: „World University Rankings" spravovaný společností Quacquarelli Symonds a proto zkráceně nazývaný QS, „Times Higher Education" (THE) podporovaný společností Elsevier, a „Academic Ranking of World Universities" (ARWU) spravovaný univerzitou Jiao Tong v Šanghaji. Všechny tyto žebříčky jsou charakteru „top", to znamená, že hodnotí globální, příp. regionální výběr nejlepších univerzit. ARWU od 1. do 500, QS od 1. do 916 a THE od 1. do 978., přičemž zhruba od 2/3 žebříčku je pořadí intervalové, např. po 10, 50, 100 a 200. I když při znalosti metodiky lze i v intervalu propočítat přesnější pořadí, tvůrci žebříčků dobře vědí, proč volí na vzdálenějších pozicích intervaly. Rozlišovací schopnost žebříčků tam není pochopitelně tak ostrá jako v čele. V globálním měřítku jasně dominují americké a britské univerzity. Na prvních pozicích ve světě se promíchávají Harward, MIT, Caltech, Stanford, Berkeley, Cambridge a Oxford. V Evropě Cambridge, Oxford, College London, ETH Zürich a Imperial College London. První francouzská univerzita je až 10. a první německá 17. Nás samozřejmě více zajímá, jak jsou na tom české univerzity. Kopíruje pořadí českých univerzit v globálních žebříčcích tradiční domácí poměry? U nás je k dispozici žebříček výzkumných institucí, který vydává Rada pro vědu, výzkum a inovace (RVVI), naposledy za rok 2014, kterému vévodí UK Praha. Máme být ovšem pyšní na české univerzity např. v evropském srovnání ? Bohužel ne, pozice českých univerzit de facto kopíruje pozici ČR v EU. UK Praha, naše největší univerzita, je v žebříčku QS Top Europe až 127.

Pozicí v globálním a respektovaném žebříčku se naše univerzity mohou chlubit, může je to šokovat, o metodice výběru si mohou myslet svoje, ale bohužel to nemohou ignorovat. Globální žebříčky jsou stále více respektovány, sledovány a komentovány nejenom v univerzitních médiích. Kromě objektivního zlepšování hodnotících parametrů vede cesta vzhůru od vyčlenění administrativní „žebříčkové" kapacity na univerzitě, přes usilovnou komunikaci se správci žebříčků, k cíli lepšího zviditelnění a „pravdivějšího" spočítání. Je bohužel smutnou pravdou, že informace o našich univerzitách jsou ve světě stále zkreslené, ale blýská se na lepší časy. Možná, že vynaložená práce se našim univerzitám zúročí, když by Vládu ČR napadlo, že v připravované Metodice hodnocení vědy 2017+ bude zohledněna jejich pozice v globálních žebříčcích a od toho odvozené peníze.

Abstrakta

Thermoresponsive polyoxazoline homopolymers and copolymers aqueous solutions studied by NMR spectroscopy

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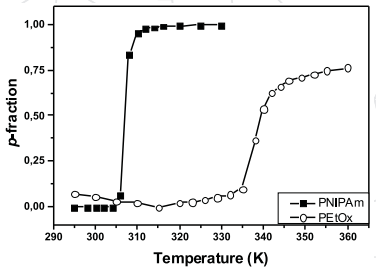
Thermoresponsive polymers are class of materials that respond to changes in temperature. Along with the changes at the macromolecular level dramatic phase or property changes occur. In last decades various thermoresponsive polymers and their derivatives, which exhibit a temperature-induced phase transition and form globules upon heating of their aqueous solutions, has attracted considerable attention [1].

The polyoxazolines (POx)s have been of great interest to researchers due to their versatility in the preparation of materials with tailor-made properties and, more recently, due to their excellent biocompatibility and tunable thermosensitive properties. It has been well established that in aqueous solution (POx)s exhibit interesting solution properties forming self-assembled structures.

We used NMR spectroscopy to study D_2O solutions of thermoresponsive poly(2-ethyl-2-oxazoline) (PEtOx) homopolymers and random copolymers PEtOx-co-poly(2-methyl-2-oxazoline) (PMeOx) of various composition. Temperature dependences of integrated intensities in high-resolution ^1H NMR spectra enabled us to determine the fraction p of polymer units with significantly reduced mobility. By series of NMR measurements we obtained temperature intervals of the phase transition for all studied samples and we found that temperature dependence of the *p*-fraction for PEtOx homopolymer shows a lower maximum value and broader transition width in comparison with frequently studied poly(N-isopropylacrylamide) (PNIPAm) (Fig. 1). For PEtOx-co-PMeOx copolymers the transitions are substantially broader and maximum values of the p-fraction significantly smaller in comparison with PEtOx homopolymer. To obtain information on behavior of water molecules during the phase transition we used measurements of spin-spin relaxation times T_2.

Acknowledgements: Support by the Czech Science Foundation (project 15-13853S) is gratefully acknowledged.

Temperature dependences of the fraction *p* of polymer units with significantly reduced mobility for PEtOx (○) and PNIPAm (■) in D_2O solutions (*c* = 5 wt%) during gradual heating.



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Abstrakta

NMR crystallography of amphidynamic MIL53(Al)–[LiCo-*bis*-dicarbollide] MOF for Li-batteries applications

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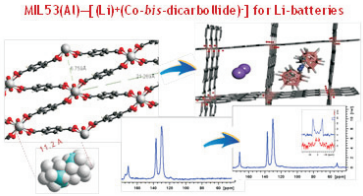
The development of hybrid and full electric vehicles raises the demand for electrical energy storage devices. However, the highest energy that can be currently stored in either batteries or supercapacitors is still insufficient. Consequently large research efforts are being devoted to the development of next-generation high-performance materials.

Inorganic building units of metal-organic frameworks (MOFs) can serve as redox active sites during the electrochemical processes. This fact together with its well-defined porous architecture that can allow Li-ions to be stored and reversibly inserted/extracted, predetermines MOFs to be explored as electrode materials for Li-batteries (LiBs). In a conversion-type MOF anode, the reversible formation or regeneration of the original MOF structure is of central importance. The selection of ligand will be crucial for the material to withstand the transformation during the conversion reactions and prevent the formation of poorly reversible oxides. In an insertion-type MOF anode, good Li storage performance can be achieved by variable-valence metal ions and/or organic ligand, rich in function groups strongly interacting with Li-ions. Robust framework with open channels to facilitate fast transport of Li-ions without damaging the MOF structure is the overarching requirement. Due to the unique pore structure that is beneficial for Li storage and good transmission of Li^+, MOFs can be also used both as positive electrodes and solid electrolyte materials. Hybrid as well as all-solid-state nanocomposite MOF-based polymer electrolytes which showed an enhanced ionic conductivity of more than two orders of magnitude at low temperature and excellent stability have shown feasibility and potential for this approach of developing new solid electrolyte materials. Many drawbacks however, still have to be overcome. MOF anodes still have problems such as poor electrical conductivity, incompleteness of the electrode reactions, large irreversible capacity loss and short life cycle. The gravimetric and volumetric Li storage capacity of the available MOF cathodes is still limited. Improvements in these fields thus require exploration of innovative electrochemistry and new concepts for material design with the help of rich MOF chemistry. A possible way how to modify MOF toward a better performance in LiBs applications is utilization of metallacarboranes.

Given their inherent robustness in a wide range of conditions, electron-delocalized skeletal bonding, amphiphilic behavior, ability to accommodate metal atoms in the cage framework, and/or their fast uniaxial rotations in a wide range of temperatures, metallacarboranes are perfect candidates for electronic applications and improved properties of MOF-based materials for LiBs. Typically, 3-$Ni^{III}(1,2\text{-}C_2B_9H_{11})_2^-$ anion undergoing reversible oxidation to the neutral species accompanied by ligand conformation transition represents a redox-driven molecular machine that has been recently used as a redox shuttle for dye-sensitized solar cells; certain salts of the type $L^+3\text{-}Co^{III}(1,2\text{-}C_2B_9H_{11})_2^-$ are semiconductors; whereas polypyrrole films doped with $Co^{III}(1,2\text{-}C_2B_9H_{11})_2^-$ show significantly improved structural stability and resistance to overoxidation.

In this contribution we demonstrate our preliminary structural investigation of a novel hybrid MIL53(Al) metallo-organic framework with uniformly dispersed Li^+[3-Co-*bis*-dicarbollide] ions exhibiting specific interactions with the framework segments and surprisingly enhanced dynamics.



Abstrakta

COMBINING LIGAND AND PROTEIN PERSPECTIVES IN FRAGMENT-BASED DRUG DISCOVERY

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Lead identification is an essential step in drug discovery process. Two main approaches are established for early stage drug development – fragment-based drug design (FBDD) and high-throughput screening (HTS). FBDD relies on weakly binding small organic molecules (often Rule of Three or Five compliant) that are elaborated (chemically modified) into more potent compounds. The biggest advantage of FBDD in comparison to HTS is that only a fraction (hundreds) of molecules are necessary to be screened against molecular target to sample even larger proportion of chemical space.[1]

First, we use a ligand observed NMR experiment - Saturation Transfer Difference (STD) to identify potential fragment hits, moreover this experiment reveals ligand binding mode. Hits are subsequently validated from the target perspective via a protein observed NMR experiment – ^{1}H-^{15}N HSQC. Combining structural data and chemical shift perturbations from HSQC provides with valuable information regarding a preferred binding site.

Here, we present hit identification against UEV domain from the ESCRT-I complex, its validation and structural characterization. The detailed insight into the UEV-ligand complex structure allows medicinal chemists to elaborate the hit into more potent lead compound.

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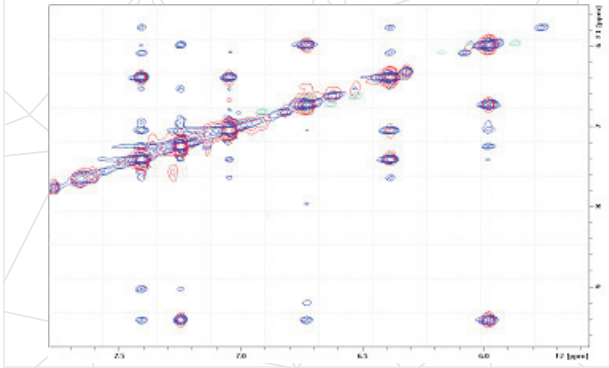

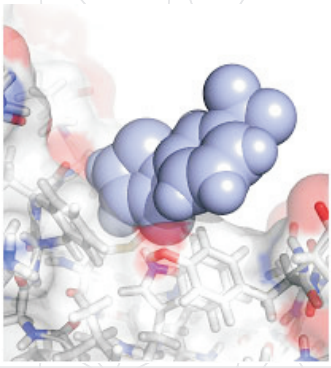

Abstrakta

SPYING ON Fe-IONS AND THEIR ROLE IN MODIFIED ALUMINOSILICATES DURING SORPTION OF ANIONS USING ssNMR SPECTROSCOPY

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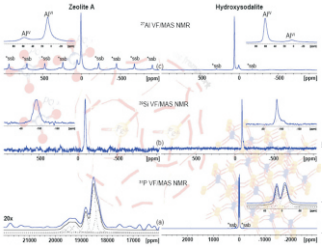
Zeolites, natural and synthetic, are aluminosilicate materials with porous structure giving them valuable properties suitable for ion exchange, sorption, catalysis, molecular sieving etc. Characteristic properties of zeolites can be changed by acid/base treatment or surfactant impregnation in order to improve separation efficiency, suitable especially for removal of anions from various solutions. Generally, modification using acid/base treatment or surfactant modification of any aluminosilicate structure may cause considerable changes in the original periodic structure and occurred changes can be monitored using X-ray powder diffraction (XRPD) and solid-state NMR (ssNMR) spectroscopies.

The $FeCl_2$ and $FeSO_4$ solutions were used for acid leaching, as aluminosilicates modified this way show high potential for removal of anions (such as As-oxyanins, PO_4^{3-} etc.) from wastewater, but also interesting catalytic properties. However, presence of Fe-ions in the zeolite matrix has substantial effect on structural characterization techniques such as XRPD and/or ssNMR spectroscopies, where the effect of fluorescence and signal vanishing has to be considered in XRPD and ssNMR spectroscopy, respectively. In this contribution simple and very effective way is demonstrated to structural description of aluminosilicate systems affected by $Fe^{II/III}$ ions using ^{27}Al, ^{29}Si MAS NMR and ^{27}Al, ^{29}Si, ^{31}P very fast (VF)/MAS NMR combined with synchronized spin-echo pulse sequence ssNMR techniques, which helps uncover mechanisms of aluminosilicates treatment using $FeSO_4$ solution and subsequent sorption of PO_4^{3-} anion from example solutions. Two different sorption mechanisms of PO_4^{3-} anions onto aluminosilicate matrix were revealed, as well as the distinct role of Fe^{3+} ions during this process. The weak acid solution of 0.3M $FeSO_4$ removes impurities from aluminosilicate matrix and subsequently causes delaumination process depending on accessible volume of individual zeolitic framework. Together with the dealumination process are diamagnetic Fe^{2+} ions oxidized to paramagnetic Fe^{3+} ions that are immobilized in inorganic framework. The role of Fe^{3+} paramagnetic species in aluminosilicate matrix was also confirmed by ADF-DFT calculations.



Abstrakta

DFT calculations of NMR parameters of framework Al atoms and extra-framework monovalent cations in silicon-rich zeolites

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Zeolites are crystalline microporous aluminosilicates that are important sorbents and catalysts. Beside the Y and USY zeolites of the faujasite structure, silicon-rich zeolites (Si/Al > 8) such as ZSM-5, the beta zeolite, ferrierite, MCM-22, and mordenite exhibit the highest industrial impact.

The positively charged catalytically active extra-framework species (protons, metal cations, and metal-oxo species) balance the negative charge of AlO_4^- tetrahedra. Silicon-rich zeolites exhibit a medium or high number of crystallographically distinguishable framework T sites occupied by Si or Al atoms. This feature, together with a low Al content, leads to a variability of the Al siting. Since counter cationic species bind to the AlO_4^- tetrahedra, the positions of Al in zeolite frameworks control the location of the active sites, which in turn affects the catalytic activity and selectivity.

A bare zeolite framework model that includes neither cations nor water molecules and has proven useful in our previous studies was adopted to calculate the local structure around the AlO_4^- tetrahedra employing periodic BLYP calculations as implemented in the cp2k program. Periodic DFT calculations including extensive molecular dynamics conformational sampling of all possible Li^+ and Na^+ sites for all the possible distinguishable Al(T) sites were performed employing the cp2k. The B3LYP ^{27}Al, ^{7}Li, and ^{23}Na NMR shielding values were evaluated utilizing the Gaussian program and seven coordination shell clusters..

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Abstrakta

Stability of framework structures of *BEA zeolite Multinuclear MAS NMR and ab initio study

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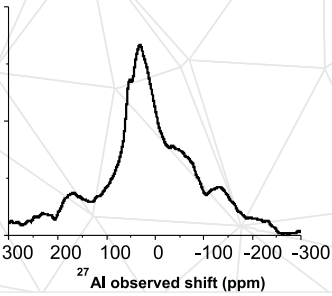
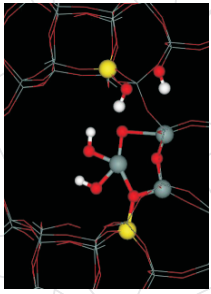
Large pore zeolite of the *BEA topology represents highly important catalyst. Zeolites crystalline microporous alumosilicate structures are in protonic form widely applied in various acid catalyzed reactions in petrochemistry. Recently, they attracted attention also as promising catalysts in the transformation of biomass.

*BEA zeolites are unique by their combination of large pore system and predominant presence of Lewis acid sites of framework Al atoms (in other zeolites prevail AlOHSi Bronstedt acid sites) in dehydrated zeolite. However, the local structure of these unique acid sites and nature of their precursors is unclear. In our study, we employed ^{27}Al MAS NMR experiment interpreted using results of quantum chemical calculations of NMR parameters of Al atoms to identify local structure of framework Al-Lewis acid sites. These sites are reflected in enormously broadened ^{27}Al resonance with C_Q = 22 MHz and isotropic chemical shift 67 ppm corresponding to trigonal planar Al atoms formed by the perturbation of the zeolite framework. Quantitative analysis of the SiOH species formed in the perturbed zeolite using ^{1}H and ^{29}Si MAS NMR experiments showed that the formation of trigonal planar Al atom is connected with partial release of one Si atom from the framework followed by the formation of a new three member ring. Framework Al-(O-Si)$_3$-O-Al sequence represent a precursor of this structure.

Catalytic transformation of biomass undergoes in aqueous environment and stability of zeolite in hot liquid water represents is essential for their application. Critical issue represents stability of framework Al atoms balancing oxonium cations in hydrated zeolite. Combination of ^{29}Si and ^{27}Al MAS NMR experiment clearly showed, that Al atoms in recently developed Al-rich beta zeolites (Si/Al $\approx$ 5) are highly stable and thus, Al-rich beta zeolite represents highly promising catalyst for the conversion of biomass. With decreasing content of Al atoms in the *BEA zeolite decreases stability of the zeolite framework and both substantial desilication and dealumination occurs.





poznámky