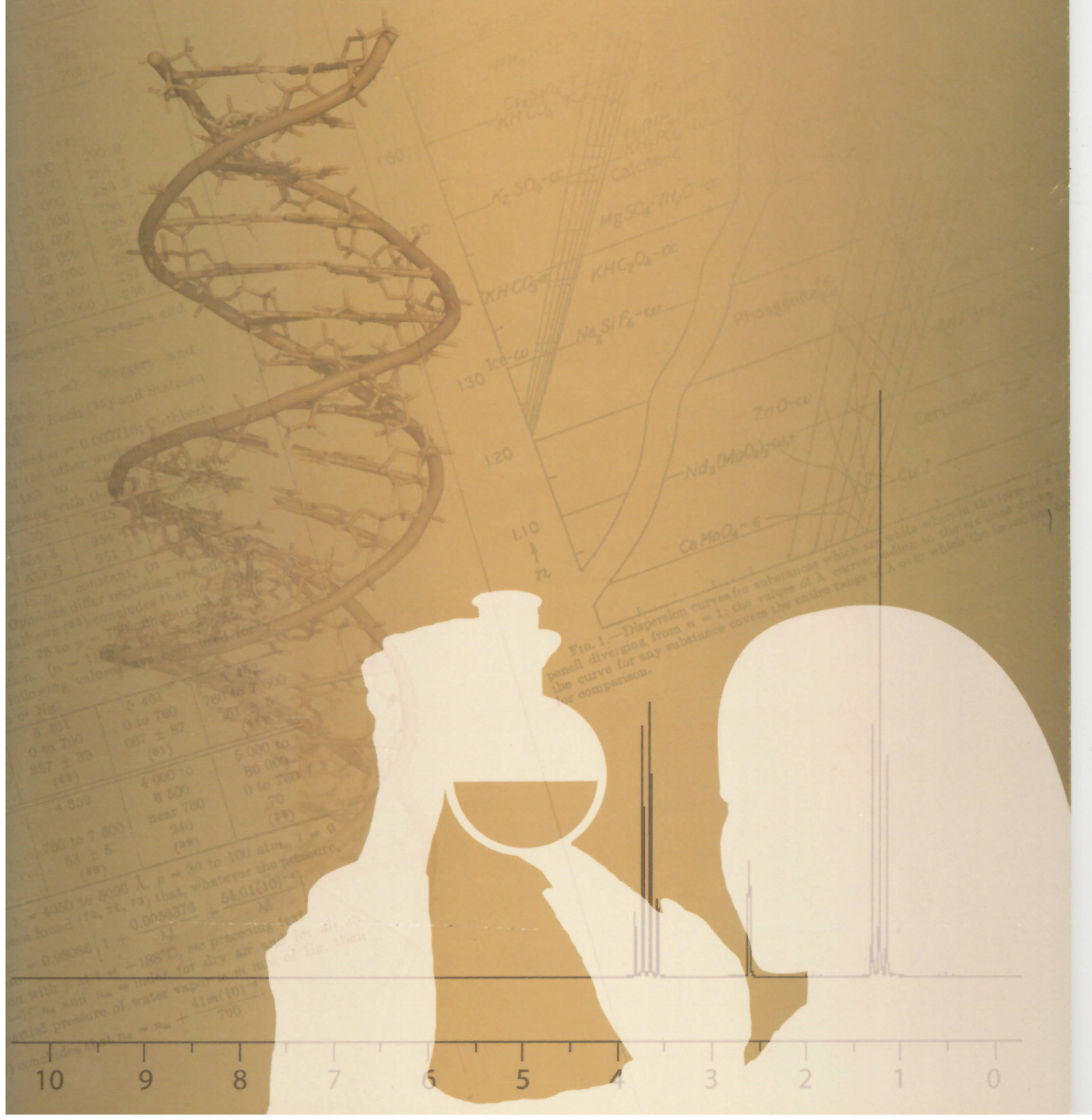
Efnafræðifélag Íslands
The Icelandic Chemical Society

Ráðstefna Efnís 2011

Efnafræðirannsóknir á Íslandi
tengsl grunnrannsókna og atvinnulífs



Dagskrá

09:00 - 09:10	Kynning	
09:10 - 09:40	Sigmundur Guðbjarnason	Saga Medica: Þegar forvitnin er drifkraftur rannsókna
09:40 - 10:10	Snorri Þór Sigurðsson	Er eitthvað spunnið í spunamerki?
10:10 - 10:30	**Kaffihlé/Veggspjöld**	
10:30 - 11:00	Oddur Ingólfsson	Hvað veldur breikkun í EBID? - Víxlverkanir lágorku-rafeinda við kóbalt tríkarbonýl nítrosýl
11:00 - 11:30	Elín Soffía Ólafsdóttir	Flókin heteroglýkön úr cýanóbakteríum – frá fléttum til Bláa lónsins
11:30 - 12:00	Guðmundur G. Haraldsson	Fituefni með háu hlutfalli ómega-3 fjölómettaðra fitusýra
12:00 - 13:00	**Hádegisverður/skrúður**	
13:00 - 13:30	Hörður G. Kristinsson	Matís: Lífefni úr hafinu - tækifæri fyrir Ísland?
13:30 - 14:00	Hilmar Bragi Janusson	Össur: Efnafræði nýsköpunar; ferli, viðhorf og tækifæri
14:00 - 14:15	Jón Otti Sigurðsson	Örfyrirlestur A - Veggspjald 21
14:15 - 14:30	Simon Klüpfel	Örfyrirlestur B - Veggspjald 15
14:30 - 14:50	**Kaffihlé/Veggspjöld**	
14:50 - 15:20	Ómar Traustason	Roche-Niblegen: Smíði á DNA örflögum og notkunar-möguleikar
15:20 - 16:00	Jón M. Einarsson	Genís: Lífvirk efni úr kítíni
16:00 - 17:00	**Veggspjaldakynningar og mixer**	
17:00 - 19:00	**Hlé**	
19:00	**Árshátíð Efnís (Sunnusalur)**	

Schedule

09:00 - 09:10	Introduction	
09:10 - 09:40	Sigmundur Guðbjarnason	Saga Medica: The role of curiosity in scientific research
09:40 - 10:10	Snorri Þór Sigurðsson	Spinning with spin labels
10:10 - 10:30	**Coffee break/Posters**	
10:30 - 11:00	Oddur Ingólfsson	Tracking down EBID broadening - Interaction of low energy electrons and cobalt tricarbonyl nitrosyl
11:00 - 11:30	Elín Soffía Ólafsdóttir	Complex heteroglycans from cyanobacteria – from lichens to the Blue Lagoon
11:30 - 12:00	Guðmundur G. Haraldsson	Lipids highly enriched with omega-3 polyunsaturated fatty acids
12:00 - 13:00	**Lunch**	
13:00 - 13:30	Hörður G. Kristinsson	Matís: Biomolecules from the ocean – opportunities for Iceland?
13:30 - 14:00	Hilmar Bragi Janusson	Össur: Roles of chemistry in innovation; processes, views and opportunities
14:00 - 14:15	Jón Otti Sigurðsson	Short lecture A - Poster 21
14:15 - 14:30	Simon Klüpfel	Short lecture B - Poster 15
14:30 - 14:50	**Coffee break/Posters**	
14:50 - 15:20	Ómar Traustason	Roche-Niblegen: DNA microarray synthesis and applications
15:20 - 16:00	Jón M. Einarsson	Genís: Chitin derived bioactive material
16:00 - 17:00	**Poster session and mixer**	
17:00 - 19:00	**Break**	
19:00	**Efnís Gala (in "Sunnusalur")**	

Ágrip fyrirlestra
Lecture abstracts

Fyrirlestur 1

Þegar forvitnin er drifkraftur rannsókna

Sigmundur Guðbjarnason, prófessor emeritus

Fjallað verður um þátt forvitni í þremur grunnransóknaverkefnum og hvernig þessi verkefni tengdust atvinnulífinu.

Fyrsta verkefnið var rannsóknir á íslenskum matvælum sem leiddu síðan til kennslu í matvælafræði við Háskóla Íslands sem hafði síðan mikil áhrif á matvælaiðnaðinn.

Annað verkefnið var rannsóknir á áhrifum lýsis og omega-3 fitusýra á hjartað og hvernig þær rannsóknir höfðu áhrif á starfsemi Lýsi hf.

Þriðja verkefnið var rannsóknir á lækningajurtum sem leiddi til stofnunar fyrirtækis til að framleiða og markaðs setja heilsubótarvörur.

The role of curiosity in scientific research

Sigmundur Guðbjarnason, professor emeritus

The role of curiosity in three basic science studies will be described and how they influenced industry.

The first was a study of Icelandic food products which led to teaching of food science at the University of Iceland influencing Icelandic food industry.

The second study was research on the influence of fish oil and omega-3 fatty acids on the heart and how this research influenced the activities of the company Lýsi hf.

The third study was on Icelandic medicinal herbs and this led to the foundation of a R&D company which produces and markets food supplements from Icelandic herbs.

Fyrirlestur 2

Er eitthvað spunnið í spunamerki?

Snorri Th. Sigurdsson

*Raunvísindasofnun, Háskóli Íslands, Dunhagi 3, 107 Reykjavík, Ísland

Leitast verður við í þessu erindi að kynna notkun á rafeindaspunatækni (electron paramagnetic resonance, EPR) við rannsóknir á byggingu og hreyfingu líffræðilegra fjölliða. Sérstaklega verður fjallað um notkun EPR við rannsóknir á kjarnsýrum. Slíkar rannsóknir krefjast staðbundinnar innleiðingar stakeinda (spunamerkja), en rannsóknahópur okkar hefur m. a. unnið að þróun spunarmerkingaraðferða fyrir kjarnsýrur á síðustu árum.

Spinning with spin labels

Snorri Th. Sigurdsson

*Raunvísindasofnun, Háskóli Íslands, Dunhagi 3, 107 Reykjavík, Ísland

Electron paramagnetic resonance (EPR) spectroscopy will be introduced in this lecture as a biophysical technique to study the structure and motion of biopolymers. In particular, the focus will be on the use of EPR to study nucleic acids. Such studies require the site-directed incorporation of persistent free radicals (spin labels). Spin labeling of nucleic acids will be described using examples of methods developed in our research group.

Fyrirlestur 3

Hvað veldur breikkun í EBID? - Víxlverkanir lágorkurafeinda við kóbalt tríkarbonýl nítrosýl

Oddur Ingólfsson

Raunvísindastofnum, Háskóli Íslands, Dunhaga 3, 107 Reykjavík

Rafeindadrifin útfelling (e. Electron Beam Induced Deposition, EBID) gerir mönnum kleift að útbúa strúktúra á nanómetraskala. Þvermáli rafeindageisla má ná niður fyrir nanómetra en útfellingin sem fæst verður alltaf töluvert breiðari. Talið er að þessi breikkun geti verið vegna dótturrafeinda með lága orku sem myndast á yfirborðinu [1]. Fáar tilraunir hafa þó verið gerðar til að styðja þessa tilgátu [2]. Því er mikilvægt að ákvarða þversnið víxlverkana rafeinda með lága orku við sameindir sem notaðar eru í EBID. Í þessum fyrirlestri verða niðurstöður mælinga á rjúfandi rafeindaálagningu (e. dissociative electron attachment, DEA) og rafeindajónun (e. electron impact ionization, EII) á $[Co(CO)_3NO]$ í gasfasa. Mælingarnar voru gerðar á þvergeislatæki, þar sem sameinda- og rafeindageislar rekast á undir réttu horni. DEA mælingarnar sýndu mikið niðurbrot við orku innsendra rafeinda á bilinu 0-9 eV [3]. Í kringum 7.3 eV rofnuðu tengi allra tenglanna og Co^- sást, þó í litlum mæli. Við lága orku myndaðist Co^+ í EII. Þessi niðurbrot eru talin geta haft áhrif á upplausn útfellinganna. Við áætluðum einnig heildarþversnið jákvæðu og neikvæðu jónanna og verða þau kynnt.

Heimildir

[1] I. Utke and J. Melngailis J. Vac. Sci. Technol. (2008) 26(4)
[2] R.N. Compton, J. A. D. Stockdale Int. J. Mass. Spectrom. Ion Phys. (1976) 22
[3] S. Engmann et al Angew. Chem. Int. Ed. (2011) 50

Tracking down EBID broadening - Interaction of low energy electrons and cobalt tricarbonyl nitrosyl

O. Ingólfsson

Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland

Electron beam induced deposition (EBID) allows fabrication of nanometer sized structures on targets of various geometries. Sub nanometer electron beam diameters can be achieved, but the resulting deposits considerably exceed this resolution. It is suggested that this broadening is caused by the low energy secondary electrons emitted from the substrate [1]. Experimental data supporting the interaction of low energy electrons with the precursor molecules, however, is very limited [2]. It is thus important to obtain the cross sections for interaction of low energy electrons with EBID precursor molecules. Here we present the results of Dissociative Electron Attachment (DEA) and electron impact ionization (EII) to gas phase $[Co(CO)_3NO]$ in an experiment with crossed electron and molecular beams. DEA studies to the metal complexes reveal a rich fragmentation pattern at incident electron energies from close to 0 eV to 9 eV [3]. In fact, multiple metal-ligand bond cleavage can be observed, yielding Co^- around 7.3 eV, though with low intensity. On the other hand, Co^+ ions are readily formed in the low energy regime during EII with high intensity. They are consequently believed to also have an impact on the deposit resolution. Estimation of the absolute cross sections for positive and negative ion fragments will be presented.

References

[1] I. Utke and J. Melngailis J. Vac. Sci. Technol. (2008) 26(4)
[2] R.N. Compton, J. A. D. Stockdale Int. J. Mass. Spectrom. Ion Phys. (1976) 22
[3] S. Engmann et al Angew. Chem. Int. Ed. (2011) 50

Fyrirlestur 4

Flókin heteróglýkön úr cýanóbakteríum – frá fléttum til Bláa Lónsins

Elín Soffía Ólafsdóttir* og samstarfsmenn

* Háskóli Íslands, Heilbrigðisvísindasvið, Lyfjafræðideild,
Hagi, Hofsvallagata 53, IS-107 Reykjavík (elinsol@hi.is)

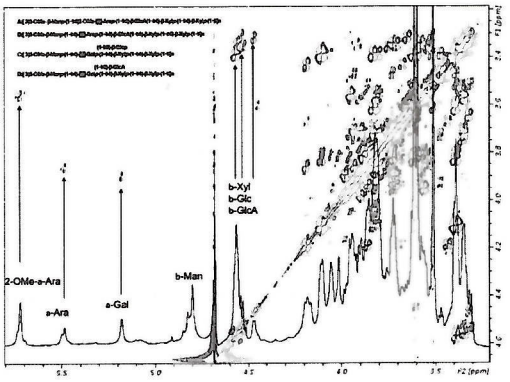
Cýanobakteríur er hópur fornra og frumbjarga örvera, sem finnast víða í Náttúrunni.

Þær framleiða fjölsykrur, svokallaðar exosykrur (EPS), sem þær seyta út í umhverfi sitt. EPS hafa verið rannsakaðar töluvert á undanförnum árum vegna áhugaverðra þykkjandi, fleytandi og biosorbent áhrifa þeirra á vatnslausnir, sem mögulega gætu nýst í líftækniiðnaði. Vitað er að EPS eru flókin, súr heteróglýkön, en þörf er á nákvæmari þekkingu á byggingum þeirra til að geta skilið sambandið á milli bygginga og eiginleika þessara nytsömu fjölliða.

Auk þess að vera áhugaverð efni til notkunar í iðnaði, þá hafa sumar fjölsykrur ýmiss konar áhrif á frumur ónæmiskerfisins og eru þekktar fyrir að hafa græðandi áhrif á húð og slímhúðir.

Rannsóknin fjallar um þrjú heteroglýkön sem voru einangruð úr þremur ólíkum cýanóbakteríum úr íslensku umhverfi: colleman úr cýanófléttunni *Collema flaccidum* [1], Nc-5-s úr landþörungi eða cýanóbakteríunni *Nostoc commune* og BLK-0 úr rækt kúlulaga cýanobakteríu sem er ríkjandi í Bláa Lóninu.

Einangrun og byggingargreining þessara heteróglýkan fjölsykra verður lýst og hún rædd. Helstu aðferðir sem notaðar voru við einangrun voru vatnsúrhlutun, etanólfelling, díalýsa, jónskiptaskiljun og gelsíun. 2D NMR kjarnsegulgreining og GC-MS einsykrugreining og greining á gerðum tengja með metýleringsanalýsu voru notuð við byggingargreiningu.



Mynd 1. 1D prótónuróf af colleman; anómer merki eru dregin fram. DQF-COSY róf er lagt ofan á 1D rófið. Bygging colleman í vinstra horni [1].

Kúlulaga cýanóbaktería (blágrænþörungur) er ríkjandi lífveras í jarðhitasjó Bláa Lónsins. Hún seytir flóknum heteróglýkan fjölsykrum, út í umhverfi sitt. Áhrif sykranna á viðbrögð ónæmiskerfisins voru rannsökuð í angafrumum í rækt og reyndust hafa áhugaverð áhrif á boðefnaprófílinn, sem hugsanlega gætu verið meðvirkandi þáttur í gagnsemi Bláa Lónsbaða við Psoriasis sjúkdómnum.

Heimildir

[1] Jensen JSRE, Petersen BO, Veselinovic T, Olafsdottir ES, Duus JO, Omarsdottir S. (2010) *Carbohydrate Polymers*; 80: 799-807

Lecture 4

Complex heteroglycans from cyanobacteria – from lichens to the Blue Lagoon

Elín Soffía Ólafsdóttir* and co-workers

* University of Iceland, School of Health Sciences, Faculty of Pharmaceutical Sciences, Hagi, Hofsvallagata 53, IS-107 Reykjavik, Iceland (elinsol@hi.is)

Cyanobacteria comprise a group of ancient photoautotrophic microorganisms that are widespread in Nature.

They produce exopolysaccharides (EPS) that have been studied considerably in recent years for their viscousifying, suspending, emulsifying and biosorbent abilities of interest for biotechnological applications. They are known to be complex acidic heteroglycans, however knowledge about the structural details of these EPS is scarce and is much needed in order to understand their chemical and physicochemical properties.

In addition to be of industrial interest, some polysaccharides have immunomodulating effects, and have been shown to direct the immune response towards either pro-inflammatory or anti-inflammatory responses.

The present studies describe cyanobacterial heteroglycans isolated from three different biosources collected in Icelandic environment: colleman from a cyanolichen [1], Nc-5-s from a colonized terrestrial cyanobacetrium and BLK-0 from the coccoid cyanobacterium from the Blue Lagoon.

The isolation and structure elucidation of the heteroglycans is described and discussed. The principal methods used are ion exchange and size exclusion chromatography, 2D NMR spectroscopy and GC-MS and methylation analysis.

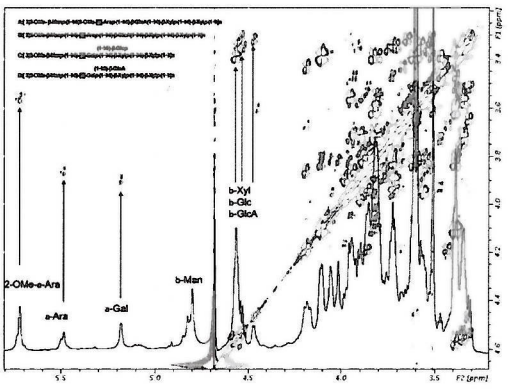


Figure 1. 1D proton spectrum of colleman with labelling of different anomeric signals overlaid with the DQFCOSY spectrum [1].

A coccoid *cyanobacteria* (or a blue-green algae) is one of the dominating life forms in the geothermal ecosystem of the Blue Lagoon. It releases a complex heteroglycan BLK-0 into its surroundings. The immunomodulating activity of these polysaccharides were investigated in the human dendritic cell bioassay and shown to have an interesting effect on the cytokine secretion profile, which might be considered to contribute to the overall clinical benefit seen for psoriasis patients bathing in the Lagoon.

References

[1] Jensen JSRE, Petersen BO, Veselinovic T, Olafsdottir ES, Duus JO, Omarsdottir S. (2010) *Carbohydrate Polymers*; 80: 799-807

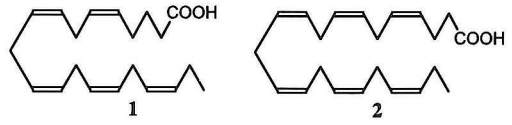
Fyrirlestur 5

Fituefni með háu hlutfalli ómega-3 fjölómettaðra fitusýra

Guðmundur G. Haraldsson

Raunvísindastofnun Háskólans, Háskóla Íslands

Um miðjan áttunda áratug seinustu aldar hófust rannsóknir við HÍ er miðuðu að því að útbúa þríglyseríð úr þorskalýsi með háu hlutfalli ómega-3 fjölómettuðu fitusýranna EPA (1) og DHA (2). Þessar rannsóknir þróuðust hratt í öflugt frumkvöðlastarf þar sem lípösum var í fyrsta sinn beitt á margvísleg esterunar- og umesterunarferli þessara eftirsóttu fitusýra við vatnssnauðar aðstæður. Þessar rannsóknir voru unnar í samvinnu við Lýsi hf og Novo Nordisk í Danmörku (nú Novozymes).



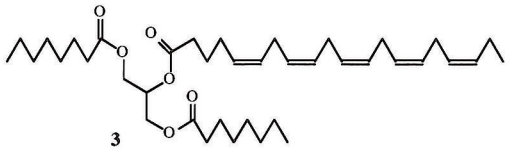
1 2

Með svipuðum aðferðum líftækni fituefna tókst að hækka hlutfall EPA og DHA umtalsvert í eterlípíðum úr hákarlalýsi og fosfólípíðum.

Í samvinnu við norsku fyrirtækin Norsk Hydro og dótturfyrirtæki þess Pronova Biocare og síðar EPAX var í framhaldinu miðað að því að útbúa þykkni EPA og DHA á formi etyl estera eða óbundinna fitusýra úr margvíslegum lýsistegundum með hraðafræðilegri aðgreiningu (kinetic resolution) fyrir tilstilli lípasa. Þarna er spilað á þann eiginleika lípasa að taka sumar fitusýrur fram yfir aðrar.

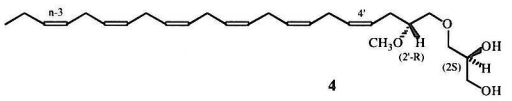
Þá var unnið að lausnum á vandamálum er tengjast lúðueldi í samvinnu við Fiskeldi Eyjafjarðar og var þróuð ómega-3 rík fitublanda sem leysti vandamál tengd þroskun lúðulirfa í seiði í samvinnu við Fiskeldi Eyjafjarðar og Lýsi hf.

Á fyrsta áratug 21. aldar var aðaláherslan lögð á efnasmíðar stöðubundinna fituefna þar sem lípasar voru notaðir til að stjórna skipan og staðsetningu fitusýra í einstakar stöður þríglyseríða og handhverfuhreinna eterlípíða og fosfólípíða. Dæmi um slíkt stöðubundið þríglyseríð er **3** hér að neðan skipað hreinu EPA í miðstöðu og miðlungslöngu fitusýrunni kapró-sýru í endastöðum.



3

Að lokum hefur áhersla undanfarinna missera síðan beinst að heildarsmíði flóknari fjölómettaðra fituefna, einkum eterlípíða af 1-O-alkyl-*sn*-glyseról gerð sem setin eru metoxylhóp á alkylkeðjunni (4).



4

Þessar rannsóknir á sviði ómega-3 fjölómettaðra fitusýra hafa getið af sér meira en tug alþjóðlegra einkaleyfa í samvinnu við þau fyrir-tæki sem getið var hér að framan.

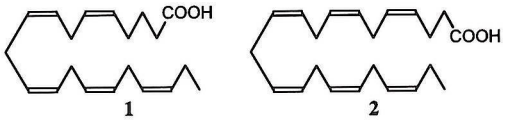
Lecture 5

Lipids highly enriched with omega-3 polyunsaturated fatty acids

Guðmundur G. Haraldsson

Science Institute, University of Iceland

In the mid 1980s research was started focusing on preparation of cod liver oil triglycerides highly enriched with the long-chain omega-3 type polyunsaturated fatty acids (n-3 PUFAs) EPA (**1**) and DHA (**2**). That research soon developed into pioneering work that involved lipase catalyzing for the first time various esterification and transesterification reactions involving the highly beneficial omega-3 PUFAs. This research was conducted in collaboration with Lysi hf in Iceland and Novo Nordisk in Denmark (now Novozymes AS).



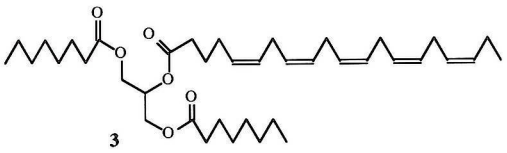
1 **2**

Similar lipid biotechnology methods resulted in significant enrichment levels of EPA and DHA in ether lipids originating from shark liver oil and phospholipids.

Collaboration with the Norwegian companies Norsk Hydro and its daughter company Pronova Biocare (now Pronova Biopharma) and later EPAX AS in Ålesund resulted in concentrating EPA and DHA as ethyl esters and free fatty acids from various fish oil types. This was based on lipase fatty acid selectivity using kinetic resolution.

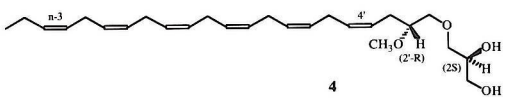
Problems that relate to halibut aquaculture and metamorphosis of halibut larva to develop into healthy juvenile fish were solved by developing a lipid feed formula offering DHA enriched marine phospholipids and highly DHA enriched triglycerides from our previous synthetic work. This was a result of a very fruitful collaboration between Fiskeldi Eyjafjarðar hf in Akureyri og Lýsi hf.

During the first decade of the 21st century the main emphasis was laid on chemoenzymatic synthesis of structured lipids utilizing lipase regioselectivity to control location of predetermined fatty acids into the various positions of the glycerol backbone in triglycerides and enantiopure ether lipids as well as phospholipids. An example is provided in triglyceride **3** possessing pure EPA at the 2-position and pure medium-chain caproic acid at the 1,3-positions of the glycerol backbone.



3

Finally, the current chief emphasis is on total synthesis of more complicated polyunsaturated lipids, especially methoxylated ether lipids of the 1-O-alkyl-*sn*-glycerol type possessing a methoxyl group located on the alkyl moiety (**4**).



4

This research in the omega-3 area has resulted in more than ten international patents that have been accomplished in collaboration with the private companies mentioned above.

Fyrirlestur 6

Lífefni úr hafinu – tækifæri fyrir Ísland?

Hörður G. Kristinsson

Matís ohf.

Hafið kringum Íslandi geymir tækifæri langt umfram hefðbundna vinnslu sjávarafurða og getur líftæknin spilað mikilvægt hlutverk í nýtingu sjávarafurða. Lífverur hafsins geyma aragrúa af lífefnum og lífvirkum efnum sem mörg hver hafa einstaka eigileika sem geta nýst á fjöldan allan hátt. Við höfum bara rétt kroppað í yfirborðið hvað þekkingu okkar varðar á möguleikunum sem liggja í íslensku lífríki. Til viðbótar við sérstakt lífríki þá fellur talsvert af aukahráefni við vinnslu sjávarafurða sem hægt er að breyta í umtalsverð verðmæti. Mörg rannsókna- og vöruþróunarverkefni með mikla nýtingarmöguleika hafa verið í gangi hjá Matís undanfarin misseri. Hér má nefna verkefni þar sem prótein eru eingangruð úr aukahráefni til að búa til verðmæt lífefni. Einnig er verið að skoða framleiðslu á lífvirkum brjóskefnum úr sæbjúgum og hákarlabrjóski. Mikil vakning er á nýtingu á þangi og þara, sem rannsóknir Matís sýna að megi geyma margþætta virkni gegn ýmsum kvillum og sjúkdómum. Einnig er unnið hörðum höndum að finna arðbærar nýtingarleiðir fyrir slóg með hjálp ensíma. Þrátt fyrir að vera lítil þá höfum við náð talsverðum árangri í rannsóknar og þróunarstarfi tengt lífefnum úr hafinu. Ef rétt er haldið á spilunum og stuðningur við greinina er nægur þá eigum við bjarta framtíð á þessu sviði. Mjög mikil aukning er á eftirspurn lífvirkra efna úr hafinu, og er enginn vafi að Ísland getur spilað stórt hlutverk þar sem uppspretta og framleiðsluland þeirra.

Biomolecules from the ocean – opportunities for Iceland?

Hörður G. Kristinsson

Matís ohf.

The ocean around Iceland holds numerous opportunities beyond traditional processing of fish products and biotechnology can play an important role here. Marine organisms contain a large number of diverse biomolecules and bioactive compounds which have unique functionality and applicability. We have just skimmed the surface regarding our knowledge on the potential that lies within marine organisms around Iceland. In addition to the many unique organisms living in the ocean, a great amount of byproducts are generated during seafood processing which can be converted into valuable products. At Matís many research and development (R&D) projects with significant potential have been conducted in the past few years. As an example, processes have been developed where proteins and peptides are extracted from byproducts to produce valuable products. Significant efforts are also directed at looking at production of valuable bioactive sugars from cartilage and chitin based materials. Lately there has been a surge of global interest in compounds from marine seaweeds and Matís has a strong research program in that area which has demonstrated some remarkable activities of these compounds. Projects are also ongoing to develop processes to produce valuable products from fish viscera with the help of enzymes. Despite being small, Iceland has made significant achievements in R&D connected to marine biomolecules. Provided we get enough support and R&D work is focused in the right areas Iceland will have a bright future in marine biomolecules. There is significant and increased global demand for marine biomolecules, and there is no doubt that Iceland can play a significant role as their source and country of production.

Fyrirlestur 7

Efnafræði nýsköpunar; ferli, viðhorf og tækifæri

Hilmar Bragi Janusson

Össur hf.

Í fyrirlestrinum verður tæpt á því hvernig fyrirtæki og grunnrannsókna teymi geta unnið saman að nýsköpun. Lýst er ferlum og hvaða hlutverki efnafræðin getur gegnt í tæknistefnu fyrirtækis. Lýst er tímalínum og viðhorfum sem gilda sem og hvaða gildrur eru til staðar. Að lokum verða nefnd dæmi um tækifæri þar sem efnafræði getur gegnt lykilhlutverki í framtíðar nýsköpun. Dæmin sem tekin eru: lyfjaflutningur í silikoni og við hámörkun eiginleika í svokölluðum magnetorheologic vökvum.

Roles of chemistry in innovation; processes, views and opportunities

Hilmar Bragi Janusson

Össur hf.

In this lecture a model is described on how cooperation of innovation between a research team and a company may look like. The roles of chemistry in the technological strategy of a company is outlined. The expectations on timelines and important attitudes are demonstrated. In addition examples are given of opportunities where chemistry could provide a valuable contribution in future innovation. The examples are on pharmaceuticals in silicone and optimization of properties in magnetorheological fluids.

Fyrirlestur 8

Roche NimbleGen – Smíði á DNA örflögum og notkunarmöguleikar

Ómar Traustason

NimbleGen hefur starfað á Íslandi síðan í febrúar 2002 og hefur vaxið jafnt og þétt þau tæpu 10 ár sem liðin eru síðan, fyrirtækið hefur alla tíð haft sterk tengsl við háskólasamfélagið bæði hérlendis sem og erlendis, þar sem allt frá upphafi hafa helstu viðskiptavinir fyrirtækisins verið rannsóknasetur og háskólastofnanir víðsvegar um heim. Árið 2007 var NimbleGen keypt af svissneska fyrirtækinu Roche, og hefur starfað síðan undir merkjum Roche sem Roche NimbleGen

Erindið mun að mestu fjalla um þá tækni sem NimbleGen nýtir til að smíða DNA örflögur ásamt því hvernig nýta má DNA örflögur sem stuðning fyrir DNA raðgreiningu.

Roche Nimblegen – DNA microarray synthesis and applications

Ómar Traustason

NimbleGen being operating in Iceland in February 2002 and since then the company has steadily expanded its operation. All thought its history NimbleGen has maintained a good relationship with Universities and Research institutions around the world that also have been the largest customer base for NimbleGen products. In 2007 NimbleGen was acquired by Swiss company Roche Diagnostics and since operated as Roche NimbleGen.

Presentation will mostly cover the technology used for manufacturing of DNA microarrays as well as how DNA microarrays can be utilized to support DNA sequencing applications.

Fyrirlestur 9

Lífvirk efni úr kítíni

Jón M. Einarsson,

Genís ehf

Frá febrúar 2005 hefur Genís ehf lagt alla sína krafta í að þróa framleiðsluferla fyrir lífvirkar sykrur úr kítíni og að skima fyrir virkni þeirra í ýmsum líffræðilegum sjúkdómsmódelum, bæði *in vitro* og *in vivo*. Megin niðurstaðan er sú að kítínefni þessi draga úr bólgum og örvefsmyndun og stuðla um leið að nýmyndun eðlilegra og starfhæfra vefja í stað þeirra sem hlutu skaða af orsökum bólgunnar. Þetta hefur ýtt undir þær hugmyndir að nota megi þessi kítínefni í meðhöndlun fjölda sjúkdóma, ýmist með inntöku um munn og meltingarveg eða með því að græða efnin inn í skaddaða vefi við skurðaðgerðir. Þróaðar hafa verið tvær meginafurðir; annarsvegar ígræðsluefni í bein (fjölsykrur; Chitobiomer^{TM}) með skurðaðgerð og hinsvegar lyfjasproti til inntöku (fáskykrur; T-ChOS^{TM}). Þá hafa verið rekin hliðarverkefni þar sem leitast er við að svifta hulunni af þeim frumulíffræðilegu og sameindafræðilegu leyndardómum sem liggja að baki þeirri mögnuðu líffræðilegu virkni sem við höfum séð í frumuræktum, vefjaræktum og í ýmsum dýramódelum fyrir mismunandi sjúkdóma. Margt af þessu hefur náðst með samvinnu við erlenda og íslenska vísindamenn. ARM-hópurinn (ARM-Consortium), þar sem ARM stendur fyrir *„Aminosugars in Regenerative Medicine"* varð til árið 2008. Innan ARM-hópsins hafa starfað um 20 íslenskir vísindamenn ásamt nemum; verkfræðingar, efnafræðingar, lífefnafræðingar, sameindaerfðafræðingar, frumulíffræðingar, læknar og dýralæknar. Innan þessa samstarfs hafa verið keyrð um 8 verkefni og sum þeirra styrkt myndarlega af Rannís. Vörur og framleiðsluferlar fyrirtækisins eru varðar einkaleyfum.

Chitin derived bioactive material

Jón M. Einarsson,

Genís ehf

From February 2005, Genis ehf has developed production methods for bioactive sugars from chitin as well as screened for their biological activity in various disease animal models *in vitro* and *in vivo*. The main result is that these chitin derived bioactive materials reduce inflammation and fibrous tissue formation as well as induce healthy tissue regeneration in diseased tissues. Two products have been developed; one a drug candidate for oral administration (oligosaccharides; T-ChOS^{TM}) treating systematically various diseases and the other product as an implanted bone healer (polysaccharide; Chitobiomer^{TM}) for *in situ* effect. Attempts have also being made to illuminate the mechanic of this remarkable chitin action, through the chitinases and chitinase like proteins, expressed in the human body, as putative receptors. This work is a fruit of long collaboration between Genis and various scientists in Iceland and abroad. Genis production methods and products are patented by the company.

Ágrip veppspjalda
Poster abstracts

Veggspjald 1

Áhrif vegna útfellingar á saltbrú á hitastöðuleika subtilasanum aqualysin I

Brynjar Örn Ellertsson*, Sigríður H. Þorbjarnardóttir†, Magnús Már Kristjánsson*

*Raunvísindastofnun Háskóla Íslands, Reykjavík, IS , †Líffræðistofnun Háskóla Íslands, Reykjavík, IS

Aqualysin I (AQUI) er mjög hitastöðugur subtilísin-líkur serín próteinasi (subtilasi) úr hitakæru bakteríunni *Thermus aquaticus*. Bygging og eiginleikar á AQUI hafa verið bornir saman við samstofna ensím lífvera sem aðlagaðar eru að kaldari aðstæðum með það að markmiði að skilja betur eðli hitastigsaðlögunar. Eitt slíkt ensím er subtilasi frá kuldakæru *Vibrio*-tegundinni PA-44 (VPR). Þessi tveir skyldu subtilasar hafa mjög líkar 3D byggingar, enn mjög mismunandi virkni og stöðuleika.

Tilgátur eru um að eitt megineinkenni hitastöðugra ensíma sé stíf myndbygging þeirra, sem felur í sér að þau ráða yfir umtalsvert lægri heildar- eða staðbundnum sveigjanleika í samanburði við samstofna miðlungs- og kuldakær prótein. Hitakær ensím hafa því venjulega yfir að ráða lágri hvötunargetu og háum hitastöðugleika. Vísbendingar eru um að aukinn fjöldi eða/og styrking saltbrúa spili mikilvægt hlutverk í aukningu hitaþolni hjá hitakærum ensímum, sem eigi sér stað með því að stífa byggingu þeirra.

Samanburður á 3.stigs byggingum AQUI og VPR leiddi okkur til að setja fram þá tilgátu að aukinn fjöldi saltbrúa spiluðu hlutverk í auknum hitastöðuleika hjá AQUI í samanburði við VPR. Til að prófa þessa tilgátu höfum við beitt markvissum stökkbreytingum til eyða nokkrum þessara saltbrúa, sem við metum að séu til staðar í AQUI en ekki í VPR. Ein þessara meintu saltbrúa er á milli amínósýruhliðarkeðja Asp98-Arg95-Asp58 í AQUI. VPR hefur bara einfalda saltbrú, Arg95-Asp58, og er með Ser í stöðu 98. Saltbrúin tengir lykkju, sem inniheldur kalsíum bindiset í VPR (Ca-2) sem er ekki til staðar í AQUI, í nálægð við hvarfefnisbindisetið. Því er spáð að þessi auka saltbrú hjálpi við að stöðga þetta svæði hjá hvarfbindisetinu í AQUI.

Hérna birtum við mælingar á eiginleikum á stökkbrigðisins Asp98Ser sem var hannað til að eyða meintu viðbótar saltbrúnni í AQUI. Stökkbrigðið var hannað með markvissri stökkbreytingu og tjáð í *E.coli*. Asp98Ser stökkbreytingin hafði umtalsverð áhrif á hraðafræðilega eiginleika ensímsins. Aukning á hverfitölunni (k_{cat}) og minnkun á Michaelis konstantinum (K_m) leiddi til 2,5 faldrar aukningar í hvötunargetu (k_{cat}/K_m) samanborið við villigerðina af AQUI sem gæti bent til þess að stökkbreytingin hafi aukið staðbundinn sveigjanleika í AQUI. Stökkbreytingin hafði ekki martæk áhrif á hitastöðuleika ensímsins.

Poster 1

The effect of elimination of salt bridges on the properties of the thermostable subtilase, aqualysin I

Brynjar Örn Ellertsson*, Sigríður H. Þorbjarnardóttir†, Magnús Már Kristjánsson*

*Department of Biochemistry, Science Institute, University of Iceland, Reykjavik, IS
†Institute of Biology, University of Iceland, Reykjavík, IS

Aqualysin I (AQUI) is a highly thermostable subtilisin-like serine proteinase (subtilase) from the thermophilic bacterium *Thermus aquaticus*. In order to gain a better understanding of the molecular mechanisms of temperature adaption of subtilases, the structure and properties of AQUI are compared to a homologous enzymes from organisms adapted to lower environmental temperatures. One such enzyme is a subtilaese from a psycshrotrophic *Vibrio*-species PA-44 (VPR). These two homologous subtilases have very similar 3D structures, but differ significantly with respect to catalytic activity and stability. It has been suggested that one of the main characteristic of thermophilic enzymes is highly rigid protein structures, with markedly lower global or local flexibility when compared to their meso- and psychrophilic counterparts. As a result thermophilic enzymes are usually characterized by low catalytic efficiency and high thermal stability. It has been suggested that the increased number of or enforced salt bridges play an important role in thermostabilization of thermophilic enzymes, hence in rigidifying their structure.

Structural comparison of AQUI and VPR led us to hypothesize that additional salt bridges may play a role in thermostabilization of AQUI. To test some of these hypotheses we have deleted some of those ion pairs, which we deem to be present in AQUI, but not in VPR, by using site directed mutagenesis. One of those putative salt bridges is between residues Asp98-Arg95-Asp58 in AQUI. VPR has a single salt bridge, Arg95-Asp58, but contains a Ser at position 98. The salt bridges links a loop, which comprises a calcium binding site in VPR (Ca-2), but which is not present in AQUI, to a part of the substrate binding site. It is predicted that the additional salt bridge may help in the stabilizing this area of the substrate binding site.

Here we report on properties of a single mutant, Asp98Ser, which was designed to eliminate the putative additional salt bridges of AQUI. The mutant was produced with site directed mutagenesis and expressed in *E.coli*. The Asp98Ser mutation had a significant effect on the kinetic parameters. An increase in the turnover number (k_{cat}) and lowering in Michaelis constant (K_m) led to a 2.5 fold increase in the catalytic efficiency (k_{cat}/K_m) compared to wild-type AQUI suggesting that mutation led to an increased flexibility at this site in AQUI. The mutation had no significant effect on the thermal stability of the enzyme.

Veggspjald 2

Lykkjusvæði í alkalískum fosfatasa úr Vibrio kaldsjávarörverru breyta mælistikum kuldaaðlögunar.

Bjarni Ásgeirsson, Manuela Magnúsdóttir and Jens G. Hjörleifsson.

Department of Biochemistry, Science Institute, University of Iceland,
Dunhagi 3, 107 Reykjavik, Iceland. (bjarni@raunvis.hi.is).

Hreyfingar á lykkjusvæðum ensíma geta stýrt hvötunarhraða (k_{cat}) þeirra, t.d. með tengslum við kvikar hreyfingar á sam-skilum undireininga. Sveigjanleiki á snertisvæði í ensímtvenndum (e. dimers) getur þannig mótað hvötunargetuna (k_{cat}/K_m) í heild. Alkalískur fosfatasi úr Vibrio sjávarörverru (VAP) er tvennd sem hvatar vatnsrof fosfórestertengja. Svipuð ensím finnast í öllum lífverum. Þetta afbrigði hefur öfgafull einkenni kuldaaðlögunar. Tvenndarformið er mjög óstöðugt gagnvart hitun, en hvötunargetan er a.m.k. 3-falt meiri en mælist fyrir alkalíska fosfatasa úr blóðheitum dýrum eða þarmagerli við sömu aðstæður. Stór yfirborðslykkja sem teygir sig yfir hina undireininguna er áberandi séreinkenni á VAP. Við höfum rannsakað hlutverk þessarar lykkju og vetnistengja sem líma hana við yfirborð hinnar undireiningarinnar með markvissum stökkbreytingum í ljósi þeirrar tilgátu, að samráð sé milli undireininga við hvötun. Við völdum staði þar sem vetnistengi virðast mynda net. Arg336 á stóru lykkjunni myndar tvö vetnistengi við atóm á Ser87 og Ser79 á minni lykkju á gagnstæðri undireiningu, sem tengjast innbyrðis með vetnistengi. Tyr355 á stóru lykkjunni myndar vetnistengi við His56, Pro57, og Glu58. Þessi afbrigði voru greind: S87A, S79G, 79G/87A, R336L og F355Y. Mælingar á stöðugleika (CD-hitastig; virkni-hitastig; flúrljómun-urea), málmjónainnihaldi, og hvötunargetu staðfesta að með því að fórna einu vetnistengi minnkar stöðugleiki ensímsins og k_{cat} eykst. Í sumum tilfellum minnkar sækni í hvarfefnið (K_M). Aukið svigrúm til hreyfinga á snertisvæði undireininganna, útslag og/eða tíðni, getur skýrt báðar breytingarnar, því amínósýrur hvarfstöðvar eru nærliggjandi. Losara-legri stórsameindin myndi gefa amínó-sýrum frá báðum undireiningum tækifæri til nýta nettengsl betur og hreyfast hraðar í takt við hærri hvötunarvirkni.

Poster 2

Loop connections in alkaline phosphatase from Vibrio marine bacterium alter indicators of cold-adaptation.

Bjarni Ásgeirsson, Manuela Magnúsdóttir and **Jens G. Hjörleifsson.**

Department of Biochemistry, Science Institute, University of Iceland,
Dunhagi 3, 107 Reykjavik, Iceland. (bjarni@raunvis.hi.is).

Loop motions linked with dynamic movement at domain boundaries are known to be rate limiting for enzyme catalysis (k_{cat}). Flexibility at interfacial dimer contacts may also influence catalytic efficiency (k_{cat}/K_m). Vibrio alkaline phosphatase (VAP) is a dimer that hydrolysis phosphoryl esters. Similar enzymes are found in all organisms. This VAP variant shows some extreme signs of cold-adaptation. The dimeric state is very temperature labile and at the same time the catalytic activity is higher than observed with alkaline phosphatases from mesophilic organisms under identical conditions. One notable feature of VAP is a large surface loop that holds the monomers together. Since cross-talk between monomers may be a factor that influences catalytic efficiency, we have studied the role of hydrogen-bonding involved in linking this large loop to the opposite monomer by site-directed mutagenesis. The sites of mutations were chosen to focus on a hydrogen-bonded cluster. Arg336 on the large loop forms two hydrogen bonds with atoms of Ser87 and Ser79 on a loop on the opposite monomer, that in turn are linked together by a hydrogen bond. Tyr355 on the large loop forms hydrogen bonds with His56, Pro57, and Glu58. Mutants S87A, S79G, 79G/87A, R336L and F355Y were analyzed. Effects on stability (CD vs.temperature; activity vs. temperature; fluorescence vs. urea), metal-ion content, and catalysis clearly confirm that removing even a single hydrogen-bond reduces dimer stability and increases k_{cat}. In some cases, K_M also increased. An increase in interfacial motional freedom, amplitude and/or rapidity, can explain both observations through effects on the active site residues nearby. A more flexible macromolecule would allow amino acids from both subunits to act even better in a networked motion to match higher turnover rates.

Poster 3

Modeling electrochemical reactions at the solid-liquid interface using DFT calculations

Egill Skúlason

Science Institute, VR-III, University of Iceland, IS-107 Reykjavik, Iceland

Charged interfaces are physical phenomena found in various natural systems and artificial devices within the fields of biology, chemistry and physics. In electrochemistry, this is known as the electrochemical double layer, introduced by Helmholtz over 150 years ago. At this interface, between a solid surface and the electrolyte, chemical reactions can take place in a strong electric field.

In this presentation, a new computational method is introduced for creating charged interfaces and to study charge transfer reactions on the basis of periodic DFT calculations [1, 2, 3, 4]. The electrochemical double layer is taken as an example, in particular the hydrogen electrode. With this method the mechanism of hydrogen gas formation from solvated protons is studied. The method is quite general and could be applied to a wide variety of atomic scale transitions at charged interfaces.

References

[1] E. Skúlason, G.S. Karlberg, J. Rossmeisl, T. Bligaard, J. Greeley, H. Jónsson and J.K. Nørskov, *Phys. Chem. Chem. Phys.*, **9** (2007) 3241

[2] J. Rossmeisl, E. Skúlason, M.E. Björketun, V. Tripkovic and J.K. Nørskov, *Chem. Phys. Lett.*, **466** (2008) 68

[3] E. Skúlason, V. Tripkovic, M. E. Björketun, S. Guðmundsdóttir, G. Karlberg, J. Rossmeisl, T. Bligaard, H. Jónsson, J. K. Nørskov, *J. Phys. Chem. C* **114**, (2010) 18182

[4] V. Tripkovic, M. E. Björketun, E. Skúlason, and J. Rossmeisl, **84** (2011) 115452

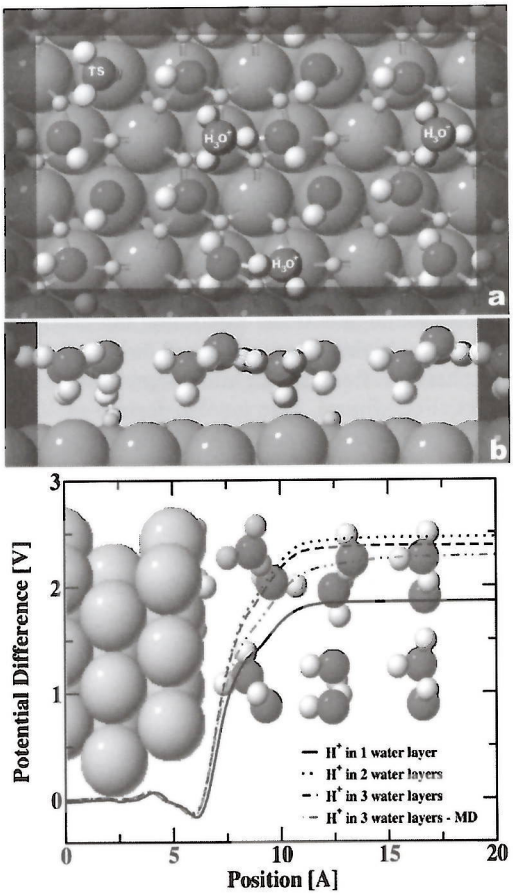


Figure 1: Simulation model setup of solvated protons in water layers above a Pt electrode. The electric potential profile mimics the nature in general details

Poster 4

Mechanism of hydrogen formation from solvated protons and electrons

Egill Skúlason

Science Institute, VR-III, University of Iceland, IS-107 Reykjavik, Iceland

The fundamental reaction of electrocatalysis is the hydrogen evolution reaction. At the interface between a solid catalyst and an electrolyte, solvated protons from the liquid and electrons from the electrode are converted into hydrogen molecules. Despite its importance, it has been debated for several decades which mechanism dominates during electrolysis. This is a complex system which poses a challenge to both atomistic simulation and experimental techniques.

Two possible mechanisms have been invoked. The solvated protons in the electrolyte start to adsorb on the surface where they combine with electrons (*Volmer step*). Then, two adsorbed H atoms on the surface may combine into an H_2 molecule (*Tafel step*). Alternatively, a solvated proton may directly react with a hydrogen atom and an electron on the surface and form an H_2 molecule (*Heyrovsky step*). Here the second proton never binds to the surface. Hence, for the overall reaction, it either needs to go via the Volmer-Tafel mechanism or the Volmer-Heyrovsky mechanism. The literature consists of conflicting reports about which mechanism is more feasible, where e.g. different mechanism has even been reported for different faces of the same metal [1].

We model the interface between a charged electrode and an ionized liquid using density functional theory (DFT) calculations [2, 3, 4]. A method is developed to vary the surface charge and the corresponding counter charge in the electrolyte.

With this new methodology we have calculated the rate of H_2 formation on several electrode surfaces in good agreement with experimental data [4]. Our conclusion about the mechanism is that the Volmer-Tafel reaction is several orders of magnitude faster than the Volmer-Heyrovsky reaction on various transition metal surfaces under typical applied electric potential [4].

We conclude the Heyrovsky pathway will never be used, on any type of electrodes, under typical applied electric potentials (around U = 0 V *vs.* NHE). These finding might have several important consequences when it comes to developing new catalysts where either hydrogen formation is desired or needs to be suppressed.

References

[1] N. M. Markovic, B. N. Grgur and P. N. Ross, *J. Phys. Chem. B* **101** (1997) 5405

[2] E. Skúlason, G.S. Karlberg, J. Rossmeisl, T. Bligaard, J. Greeley, H. Jónsson and J.K. Nørskov, *Phys. Chem. Chem. Phys.*, **9** (2007) 3241

[3] J. Rossmeisl, E. Skúlason, M.E. Björketun, V. Tripkovic and J.K. Nørskov, *Chem. Phys. Lett.*, **466** (2008) 68

[4] E. Skúlason, V. Tripkovic, M. E. Björketun, S. Guðmundsdóttir, G. Karlberg, J. Rossmeisl, T. Bligaard, H. Jónsson, J. K. Nørskov, *J. Phys. Chem. C* **114**, (2010) 18182

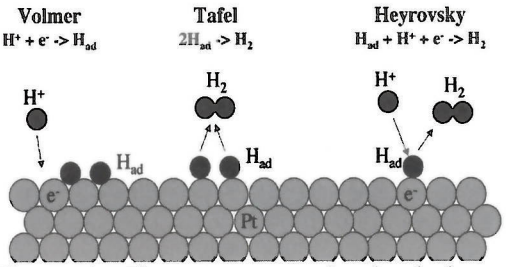


Figure 1: Elementary steps in the hydrogen evolution reaction (HER), from solvated protons in liquid and electrons in the electrode.

Poster 5

Can we produce ammonia with a mechanism similar to that of nitrogen fixing enzymes?

Egill Skúlason

Science Institute, VR-III, University of Iceland, IS-107 Reykjavik, Iceland

The process used in the chemical industry today to produce ammonia is the one invented a century ago by Haber and Bosch where nitrogen and hydrogen gas is reacted at high temperature and pressure over an iron or ruthenium catalyst. In this process, the NN triple bond is the first one to be ruptured (*dissociative mechanism*). Bacteria containing the enzyme nitrogenase, however, manage to react nitrogen molecules with protons and electrons to form ammonia at ambient conditions with the use of chemical energy stored in ATP molecules. There, the NN bond is the last to be ruptured (*associative mechanism*).

Simulation studies of the possibility of forming ammonia electrochemically at ambient temperature and pressure are presented [1]. Density functional theory calculations have been used in combination with a simple model [2] for describing the effect of applied potential to calculate the free energy profile for the electro-catalytic reduction of N_2 molecules into ammonia. Trends in catalytic activity are obtained for a range of pure transition metal surfaces using previously established scaling relationships [3]. The results indicate that ammonia may be synthesized (in higher yields than its competitive reaction, H_2 formation) at sufficiently negative applied potential, especially at electrode surfaces of Sc, Y, Ti, and Zr via the dissociative mechanism.

References

[1] E. Skúlason, T. Bligaard, S. Gudmundsdóttir, F. Studt, J. Rossmeisl, T. Vegge, H. Jónsson, and J. K. Nørskov, *submitted to PCCP* (2011)

[2] J. K. Nørskov, J. Rossmeisl, A. Logadóttir, L. Lindqvist, J. R. Kitchin, T. Bligaard, and H. Jónsson, *J. Phys. Chem. B* **108** (2004) 17886.

[3] F. Abild Pedersen, J. Greeley, F. Studt, J. Rossmeisl, T. Munter, P. Moses, E. Skúlason, T. Bligaard, and J. Nørskov, *Phys. Rev. Lett.*, **99** (2007) 016105.

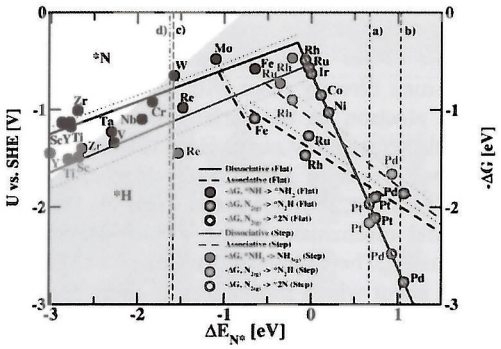


Figure 1: Volcano plots for the ammonia formation.

Poster 6

Charge and Density of States using Bader Decomposition for N_2 and CO_2 Adsorbed on Electrode Surfaces

Egill Skúlason

Science Institute, VR-III, University of Iceland, IS-107 Reykjavik, Iceland

An atomic scale simulation of electrochemical processes is an important and growing research area. While electrochemistry has played a vital role in the development and formulation of chemical concepts, modern atomic scale studies of electrochemical processes have been rather limited. On the experimental side, the challenge is to characterize processes at a solid/liquid interface as a function of applied voltage but this is a complex system where few experimental techniques can be applied. On the theoretical side, simulations of such systems require an accurate description of the electronic properties of models including a large number of atoms.

One of the basic questions is how applied voltage affects the binding of molecules to the electrode surface. Such calculations have been carried out by applying a constant electric field using a sawtooth external potential. Alternatively, one can apply an external potential to set up a potential difference between the two sides of the simulated slab and, thereby, establish a chemical potential difference for the electrons on the two surfaces of the slab. The slab then represents both the cathode and the anode. We apply both techniques in this study and compare the results for N_2 and CO_2 adsorption. In order to analyze the effects of either external potential or electric field, a decomposition of the continuous electron density in the system is needed to extract useful indicators of charge transfer and modifications of chemical properties. We have made use of the charge density decomposition defined by Bader and we describe our implementation of charge and local density of state (DOS) analysis within regions assigned to atoms and/or molecules. There, dividing surfaces placed along minima in electron density are used to divide space into regions associated with atoms and/or molecules. More precisely, the dividing surfaces are placed in such a way that the gradient of electron density has zero component normal to the surface, i.e. zero-flux surfaces.

Electric charge and partial density of states in regions defined for individual atoms and molecules using grid based Bader analysis is presented for N_2 and CO_2 adsorbed on a platinum electrode as a function of applied voltage or electric field [1]. When the density of states is projected onto Bader regions, the partial densities of states for the various subregions correctly sum up to the total density of states for the whole system, unlike the commonly used projection onto spheres which results in missing contributions from some regions while others are over counted, depending on the radius chosen. The electrode is represented by the missing row reconstructed Pt(110)-(2x1) surface to model a micro-facet boundary on the surface of a catalyst cluster. The effect of the applied voltage on the two types of admolecules is quite different but in both cases a certain voltage and electric field window leads to strong adsorption.

References

[1] S. Gudmundsdóttir, W. Tang, J. B. Maronsson, G. Henkelman, H. Jónsson and E. Skúlason, *to be submitted* (2011)

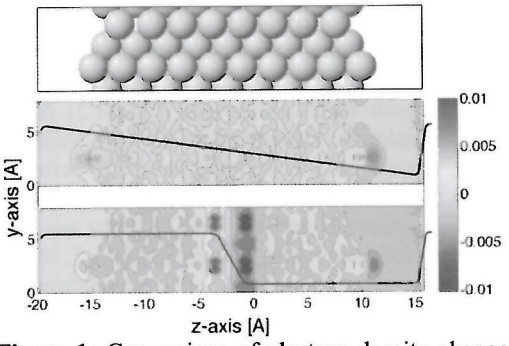


Figure 1: Comparison of electron density change when applying either electric field or a potential drop.

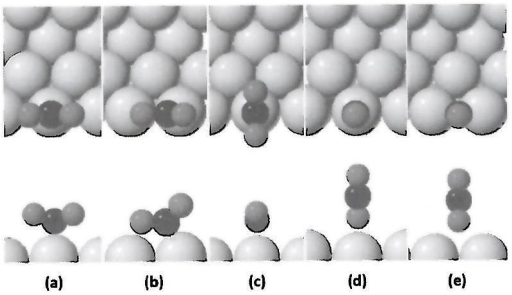


Figure 2: Adsorption configurations of CO_2 on the Pt(110) electrode when different electric fields are applied.

Poster 7

Hydrogen diffusion on transition metal surfaces

Lilja Kristinsdóttir and Egill Skúlason

Science Institute, VR-III, University of Iceland, IS-107 Reykjavik, Iceland

Diffusion of hydrogen atoms on metal surfaces is an important process and necessary for many catalytic reactions, such as the electrochemical H_2 formation, hydrogenation of nitrogen to form ammonia in the Haber-Bosch process, or when converting carbon containing species (e.g. CO_2) into useful chemicals (e.g. methanol). The H diffusion has been studied on several metal surfaces, both experimentally and theoretically [1]. H diffusion on metal surfaces has been a model system where the focus has especially been on studying the quantum nature of the hydrogen nuclei. Since the hydrogen nuclei is light, quantum effects can be observed at elevated temperatures.

Density functional theory calculations of the diffusion of hydrogen atoms on 23 transition metal surfaces in their closed-packed structure have been carried out [2]. The d-metals chosen are all the metals in the 4th, 5th and 6th period, from Sc to Au, except Mn, Tc, and Hf. Potential energy surfaces of H atom on these metals are constructed (Figure 1) and the diffusion barrier from one minima to another is compared with nudged elastic band calculations (Figure 2). Most of the minimum energy paths are parabolic in shape, except on few surfaces where hyperbolic shape is observed (Mo and Os), or a dip in the bridge position (W and Pt). Trends in the adsorption and activation energies are observed where the former is explained with the d-band model. All the activation energies for diffusion are relatively low, or from 0.04 eV for Pt to 0.28 eV on Y and Zr. Finally, we estimate the temperature where tunneling effects should start to take place.

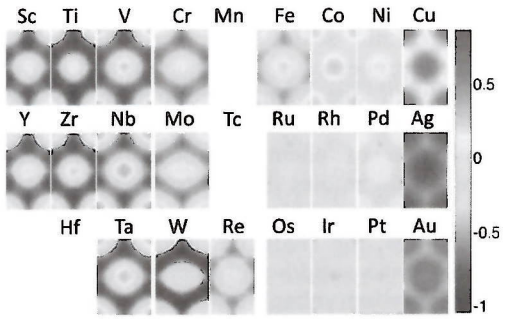


Figure 1: PES for hydrogen on transition metal surfaces relative to H_2 in gas phase.

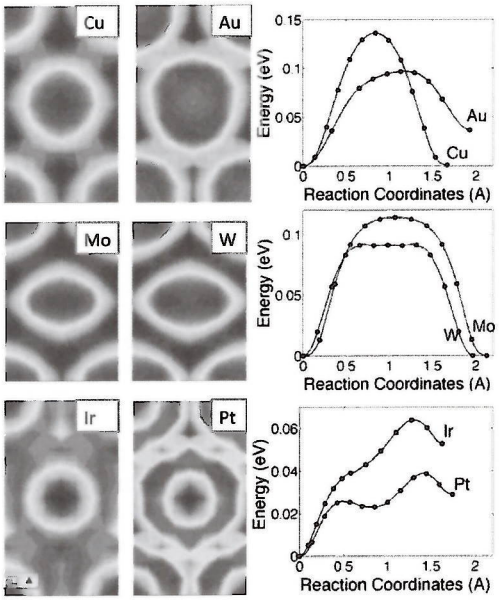


Figure 2: a) PES for hydrogen relative to H_2 in gas phase for few selected metals. The figures for each metal have different scales in order to analyze the PES profile better. b) NEB curves for the metals in a) from FCC hole to HCP hole (hole to hole for BCC metals) through the bridge site.

References

[1] S.C. Badescu and P. Salo and T. Ala-Nissila and S.C.
Ying and K. Jacobi and Y. Wang and K. Bedurftig and G. Ertl, *Phys. Rev. Lett.* **88** 136101 (2002).
[2] L. Kristinsdóttir and E. Skúlason, *to be submitted to Surface Science* (2011)

Poster 8

Mechanism of Hydrogen Gas Formation at Platinum Surfaces

S. Guðmundsdóttir, E. Skúlason and H. Jónsson

Science Institute, University of Iceland, VR-III, 107 Reykjavík, Iceland

The interaction of hydrogen with the surface of platinum metal is of fundamental importance to a wide range of technologies including various catalytic reactions, hydrogen storage, electrolysis and fuel cells [1]. The metal is typically dispersed in small clusters embedded in a matrix and the active sites are likely the edges between facets on the clusters. We have chosen to study the Pt(110)1x2 surface since it represents a realistic model for such edge sites. The desorption of hydrogen from the various sites on the surface as well as diffusion along the surfaces has been studied using density functional theory (DFT) calculations and harmonic transition state theory [2]. On this surface, the hydrogen atoms can bind to 3 different sites, with the bridge site on the top most ridge giving the strongest binding at low coverage and the bridge site in the trough giving the weakest binding to the surface [3]. The calculations of the energy barrier for H_2 desorption have given unexpected results and led to new interpretation of measured results obtained with temperature programmed desorption (TPD), a commonly used experimental technique in surface science. Up to now, it has been assumed that different peaks in a TPD spectrum give information about desorbtion directly from different types of binding states, with the peak at the lowest temperature corresponding to the state with the lowest binding energy, etc. The desorption of H_2 from the Pt(110)1x2 surface would then first come of the binding site in the trough, then from the site on the (111) facet and finally of the strong binding site on the ridge. However, based on our calculations, hydrogen first desorbs from the ridge, followed by desorption from the (111) facet and then, finally, again desorption from the ridge after hydrogen diffusion on the surface, see figure 1. This is because of anomalously strong coverage dependence of the binding energy which includes attractive interaction between adsorbed hydrogen atoms on the ridge, and lack of catalytic action in the trough. This suggests that the observed 3 different peaks of the TPD spectra for this system *can not* be interpreted as a direct desorption from each of the 3 different binding sites.

An interesting feature of the calculated minimum energy path of ridge desorption is an intermediate minimum corresponding to the formation of a Kubas complex where an intact molecule with an elongated H-H bond of 0.9 Å, and a binding energy of 0.04 to 0.2 eV (see figure 2), depending on hydrogen coverage on the surface, is observed.

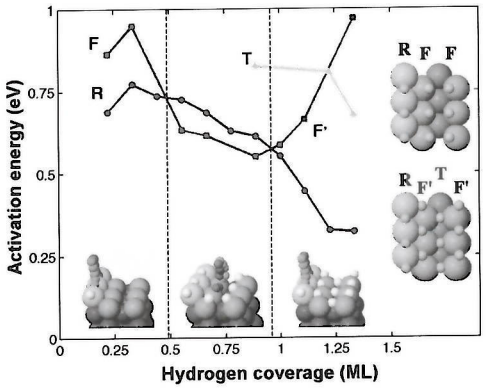


Figure 1 Calculated activation energy for desorption of H_2 as a function of coverage. The insets show the labeling of the binding sites and minimum energy paths for desorption.

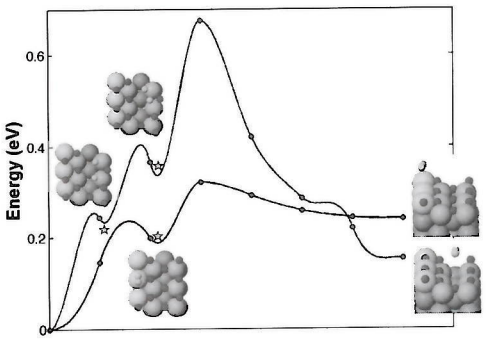


Figure 2 Minimum energy path for desorption of H_2 from ridge (blue curve) and from trough (red curve). The desorption from the ridge has a lower activation energy even though the final state is of higher energy as compared with desorption from the trough.

References

[1] E. Skúlason, V. Tripkovic, M. E. Björketum, S. Guðmundsdóttir, G. Karlberg, J. Rossmeisl, T. Bligaard, H. Jónsson and J. K. Nørskov, J. Phys. Chem. C **114**, (2010) 18182.

[2] S. Gudmundsdottir, E. Skúlason and H. Jónsson, submitted to Phys. Rev. Letters (2011).

[3] M. Minca *et al.*, Topics in Catalysis **46**, (2007)

Poster 9

Two-Dimensional (2+n) REMPI spectroscopy of CH_3Br: Rydberg states and Photofragmentation Channels

Victor Huasheng Wang, Jingming Long and Ágúst Kvaran

Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavik, Iceland

Mass spectra are recorded for (2 + n) one-colour resonance enhanced multiphoton ionization (REMPI) of CH_3Br [1] and CF_3Br as a function of resonance excitation energy to obtain two-dimensional REMPI (2D REMPI) data for the 66000-81000cm^{-1} and 71320-84600 cm^{-1} regions, respectively. Signals due to resonance transitions from the zero vibrational energy levels of the ground states to a number of Rydberg states and/or various vibrational states were identified. Various photodissociation channels were identified from atom and molecular fragment REMPI signals and ion signal power dependence data.

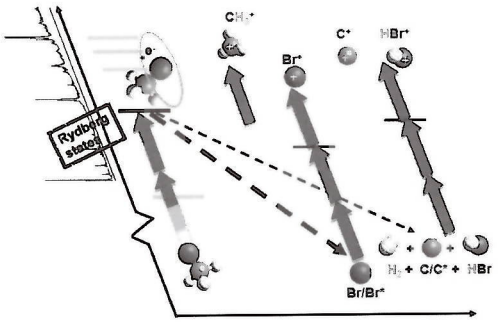


Figure 1. Schematic energy diagram relevant to CH_3Br^+, C^+ and HBr^+ channels

References

[1] Ágúst Kvaran, Kristján Matthíasson and Huasheng Wang, Andras Bodi, J. Phys. Chem. A (2010), Vol.114, 9991

Poster 10

Two-Dimensional (2+n) REMPI Spectroscopy: State Interactions, Photofragmentations and Energetics of The Hydrogen Halides

Jingming Long, Victor Huasheng Wang and Ágúst Kvaran

Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavik, Iceland

Mass spectra are recorded for one-colour (2 + n) resonance enhanced multiphoton ionization (REMPI) of HX (X=Cl, Br)[1-3] as a function of resonance excitation energy to obtain two-dimensional REMPI data. Perturbations due to Rydberg to ion-pair state interactions show as line shifts, ion signal intensity variations as well as bandwidth broadenings depending on rotational quantum numbers J′. The data allow determination of parameters relevant to the nature and strength of state interactions as well as dissociation and ionization processes. Alterations in X^+ and HX^+ signal intensities prove to be very useful for spectra assignments.

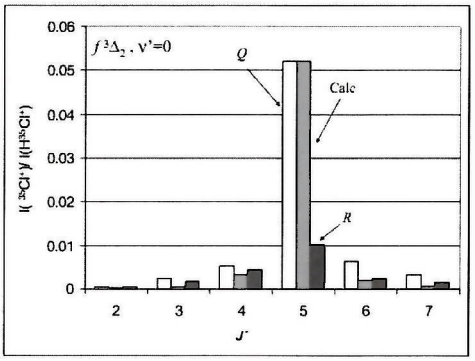


Figure 1. Comparison of experimental data and calculations for signal intensity ratios.

References

[1] Ágúst Kvaran, Kristján Matthíasson and Huasheng Wang, J. Chem. Phys (2009). 131 (4). 044324.
[2] Kristján Matthíasson, Huasheng Wang and Ágúst Kvaran, J. Mol. Spec. (2009), 255 (1), 1-5.
[3] Kristján Matthíasson, Jingming Long, Huasheng Wang and Ágúst Kvaran , J. Chem. Phys. (2011) 134, 164302.

Poster 11

The Role of Dissociative Electron Attachment in Focused Electron Beam Induced Processing

Sarah Engmann*, Michal Stano†,Štefan Matejčík†, Oddur Ingólfsson*

*Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavík, IS
†Department of Plasma Physics, Comenius University, Mlynska dolina F2, 84248 Bratislava, SK

Various molecules show the ability to resonantly capture free electrons at low energies. Subsequent dissociation of the temporary negative ion (TNI) into thermodynamically stable fragments is known as dissociative electron attachment (DEA, eq. 1).

$$MX + e^- \rightarrow [MX]^{-*} \rightarrow M + X^- \quad (1)$$

DEA hereby competes with the decay of the TNI via re-emission of the electron, i.e., autodetachment, and radiative cooling.
Trimethyl(methylcyclopentadienyl) platinum ($MeCpPtMe_3$, figure 1) belongs to the important class of organometallic precursor molecules used in focused electron beam induced processing (FEBID). Initially discovered as an unwelcome side effect in electron microscopy [1], FEBIP has quickly been embraced as a clean and precise tool for manipulating and controlling matter on a small scale. A focused, high-energy electron beam is used to locally dissociate adsorbed precursor molecules. Ideally, a chemically and structurally well-defined deposit is left behind while volatile fragments are pumped away. Although FEBIP is generally considered a high energy electron process, limitations in spatial resolution and deposit purity have drawn attention to secondary processes induced by scattering of the primary electron beam on the substrate [2]. Secondary electron (SE) emission peaks at energies below 15 eV, where DEA becomes an available dissociation pathway. Further, the yield of SEs can be close to 0.1 SEs per primary electron per electron volt [2]. Recently, we reported the absolute DEA cross-sections of cobalt tricarbonyl nitrosyl which were shown to reach values above 10^{-16} cm^2 [3]. Combining the high DEA cross sections with the high SE yield, it is believed that DEA is capable of influencing the properties of FEBIP deposits significantly. To further illustrate the effects of low energy electrons on FEBIP precursor molecules, results of a study on $MeCpPtMe_3$ will be presented. Two recent studies have focused on the effects of electron irradiation (3-500 eV) on $MeCpPtMe_3$ adsorbed onto a substrate [4, 5]. To close the gap at the low energy end and thus provide further insight into the interactions of $MeCpPtMe_3$ with low energy electrons, we have conducted a gas phase DEA study in the energy range of close to 0 to 14 eV. While no absolute cross sections could be deduced for this compound, the relevance of relative data is discussed along with the limitations of the current experimental setup.

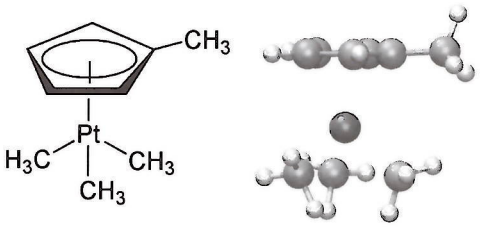


Figure 1. Trimethyl(methylcyclopentadienyl) platinum:$MeCpPtMe_3$

References

[1] A. Ennos, Br. J. Appl. Phys. (1953) vol. 4, 101.

[2] I. Utke *at al*, J. Vac. Sci. Technol. B (2008) vol. 26, 1197.

[3] S. Engmann *at al*, Angewandte Chemie Int. Ed. (2011) vol. 50, 9475.

[4] J.D. Wnuk *at al*, J. Phys. Chem. C (2009) vol. 113, 2487.

[5] M.N. Hedhili *at al*, J. Phys. Chem. C (2009) vol. 113, 13282.

Poster 12

Investigation of the synergetic effects of diammine-dichloroplatinum(II)-compounds and UVB radiation on the single strand cleavage in plasmid DNA

A. Piekarczyk, Eiríkur Stephensen, O. Ingólfsson

University of Iceland and Science Institute, Dunhaga 3, 107 Reykjavík, Iceland

The wide use of cisplatin (CDDP) in cancer treatment has made it a common object of research during the last four decades [1]. The bulk of these studies focus on cisplatin-DNA-interaction. In cancer treatment cisplatin is distributed to all body tissues [2], hence also to the skin. Furthermore, as the skin is commonly exposed to sunlight and thus UVB radiation the interaction of UVB light with cisplatin-DNA-complexes is of general interest in cancer treatment. However, to our knowledge no studies have been conducted so far, that deal with the synergic effects of cisplatin and UVB when DNA damage is induced through UVB radiation.

Here we present a study on the extent of the damage caused in plasmid DNA through broadband UVB irradiation alone and through broadband UVB irradiation when the plasmid DNA has been incubated with low doses of cisplatin. For comparison we have also studied the effect of UVB irradiation on plasmid DNA that has been incubated with the toxic, but chemotherapeutically inactive trans stereoisomer, transplatin.

We use supercoiled (CCC) pUC19 plasmid DNA as the model system. The aqueous solution of the plasmid DNA was incubated with low doses of cisplatin or transplatin and subsequently exposed to UVB broadband radiation (λ_{max}= 300 nm) over 4h. Samples were take from the solution after 1h, 2h and 4h of irradiation and analyzed using agarose gel electrophoresis. If single strand breaks (ssb) take place, the supercoiled DNA is transformed into the open circular form (OC), which has a different electrophoretic mobility. This is thus a convenient method for relative quantification of the extent of damage inflicted. The gels were scanned and the ratio between CCC and OC forms determined using an image processing software.

Cisplatin samples show a significant increase of single strand breaks after UVB irradiation compared to transplatin and the reference group.

References

[1] Lippert, Bernhard (ed.) (1999): Cisplatin: Chemistry and Biochemistry of a Leading Anticancer Drug. Wiley-VCH, Weinheim

[2] Th. G. M. H. Dikhoff, J. Radioanal. Nucl. Chem. (1998) vol. 236

Veggspjald 13

Rjúfandi rafeindaálagning á CF_4 könnuð með hraðasneiðmyndun

F. Ómarsson* O. Ingólfsson* N. Mason† E. Krishnakumar‡

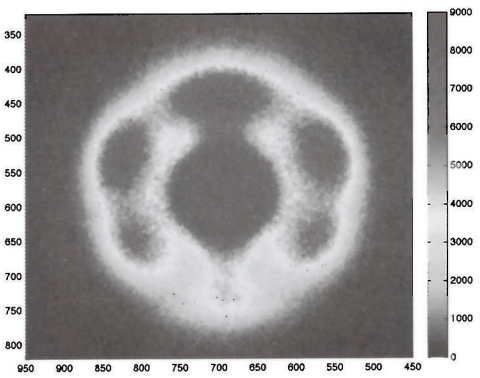
*Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland
†Dept. of Physics and Astronomy, The Open University, Walton Hall, MK7 6AA, Milton Keynes, UK
‡ Tata Institute of Fundamental Resarch, Homi Bhabha Road, Colaba, Mumbai 400005, India

Þegar hlutlaus sameind grípur rafeind myndast skammlíf neikvæð jón. Þessi skammlífa neikvæða jón myndast yfirleitt í örvuðu titringsástandi og leitar strax leiða til að slaka. Það getur hún, í sumum tilfellum, með niðurbroti sem gefur neikvætt hlaðna ögn og eina eða fleiri óhlaðnar agnir. Þetta ferli er kallað rjúfandi rafeindaálagning. Með nýlegri aðferð, hraðasneiðmyndun (e. velocity slice imaging), má fá upplýsingar um horndreifingu hlöðnu agnarinnar sem og um hreyfiorkuna sem niðurbrotin fá í ferlinu [1].

Mælingarnar eru gerðar á tæki þar sem sameindir og rafeindir lenda í áreksti undir réttu horni og þær jónir sem svo myndast greindar með flugtímamassagreini. Á enda massagreinisins er staðsetningarnæmur nemi. Spennan á nemanum er púlsuð svo mögulegt er að nema aðeins þunna sneið af Newton-kúlunni sem hver jón myndar. Með því að velja sneið í gegnum miðju Newton-kúlunnar fást upplýsginar um horndreifingu jónanna ásamt hreyfiorku þeirra [1].

Með því að nota fræðilega útreikninga frá O'Malley og Taylor [2] og samhverfuskilyrði frá Dunn [3] má sýna fram á að horndreifing jóna tvíatóma sameinda sem myndast með rjúfandi rafeindaálagningu eru háð upphafs- og lokaástöndum sameindarinnar. Þetta hefur verið aðlagað að fjölatóma sameindum af Azira *og* fél. [4].

Á þessu veggspjaldi kynnum við hraðasneiðmyndamælingar á CF_4 og berum mælda horndreifingu saman við reiknaða. CF_4 sýnir tvo toppa í rjúfandi rafeindaálagningu, annan með miðju við 6,8 eV sem gefur CF_3^- og F^- með háa hreyfiorku og hinn með miðju í 7,7 eV sem gefur einungis F^- með lága hreyfiorku. Horndreifing þessara jóna hefur verið mæld áður af Le Coat *og* fél [5], en þeir notuðu snúnginsborð sem gefur einungis niðurstöður á hornbilinu frá 20°-160° m.t.t. rafeindageislans en með hraðasneiðmyndun fæst horndreifinginn allan hringinn, 360°.



Mynd 1. Hraðasneiðmynd F^- með orku innsendrar rafeindar við 8.0 eV. Hringlaga dreifingin í miðjunni er vegna F^- jóna með lága hreyfiorku en sú ytri vegna jóna með hærri hreyfiorku.

Heimildir

[1] D. Nandi *og* fél. 2005 *Rev.* Sci. Instrum **76** 053107

[2] T. F. O'Malley and A. S. Taylor 1968 *Phys.* Rev. **176** 207

[3] G. H. Dunn 1962 *Phys.* Rev. Lett. 8 62 **8** 62

[4] R. Azira *og* fél. 1979 *J.* Phys. B: At. Mol. Opt. Phys. **12** 679

[5] Y. Le Coat *og* fél. 1994 *J.* Phys. B: At. Mol. Opt. Phys. **27** 965

Poster 13

Dissociative electron attachment to CF_4 probed by Velocity Slice Imaging

F. Ómarsson* O. Ingólfsson* N. Mason† E. Krishnakumar‡

*Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland
†Dept. of Physics and Astronomy, The Open University, Walton Hall, MK7 6AA, Milton Keynes, UK
‡ Tata Institute of Fundamental Resarch, Homi Bhabha Road, Colaba, Mumbai 400005, India

When an electron attaches to a neutral molecule a Transient Negative Ion (TNI) is formed. This TNI is generally formed in a vibrationally excited state and is bound to relax. Relaxation can occur through a dissociative channel leading to formation of a charged moiety and one or more neutral counterparts. This is termed Dissociative Electron Attachment (DEA). Using the recently developed Velocity Slice Imaging (VSI) technique it is possible to get information on the angular distribution of the charged fragment as well as the kinetic energy release in the process [1].

The apparatus consists of crossed electron and molecular beams and a Time of Flight mass spectrometer with a position sensitive detector. The detector voltage is pulsed so a thin slice of the Newton sphere of fragments can be chosen at a time. By choosing the central slice of the Newton sphere one can obtain information on the angular distribution of ionic fragments as well as on the kinetic energy released in the process.

Using theoretical calculations from O'Malley and Taylor [2] and symmetry arguments from Dunn [3], it has been shown that the angular distribution of fragments from diatomic molecules formed in DEA depends on the initial and final molecular states. This has been adopted for polyatomic molecules by Azira *et* al [4].

We present the results of VSI measurements on CF_4 and determine the molecular states involved by comparing the expermiental angular distribution with calculated angular distribution. CF_4 has two resoances, one centered at 6.8 eV yielding high kinetic energy CF_3^- and F^- and the other centered at 7.7 eV yielding low kinetic energy F^-. The angular distribution of these fragments has been measured before by Le Coat *et* al [5] using the conventional turntable arrangement which has the limited angular range of 20°-160° with respect to the electron beam compared to the whole 360° range for VSI.

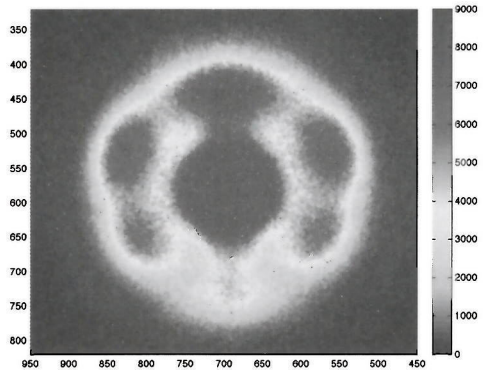


Figure 1. The Velocity Slice Image for F^- at 8.0 eV electron energy. The symmetric distribution in the center is due to low kinetic energy F^-.

References

[1] D. Nandi *et* al 2005 *R*ev. Sci. Instrum **76** 053107

[2] T. F. O'Malley and A. S. Taylor 1968 *P*hys. Rev. **176** 207

[3] G. H. Dunn 1962 *P*hys. Rev. Lett. 8 62 **8** 62

[4] R. Azira *et* al 1979 *J.* Phys. B: At. Mol. Opt. Phys. **12** 679

[5] Y. Le Coat *et* al 1994 *J.* Phys. B: At. Mol. Opt. Phys. **27** 965

Veggspjald 14

Tengjamyndanir og umröðunarhvörf í RRÁ tilraunum

B. Ómarsson*, E. H. Bjarnason*, S. Haughey†, O. Ingólfsson*, T. A. Field†

*Raunvísindastofnun, Háskóli Íslands, Dunhaga 3, 107 Reykjavík, Ísland
†School of Mathematics and Physics, Queen's University Belfast, Belfast BT7 1NN, Northern Ireland, UK

Víxlverkan sameinda og lágorkurafeinda er lýst með ófjaðrandi árekstrum sem geta leytt til sundrunar á sameindinni í gegnum ferli sem kallast rjúfandi rafeindaálagning (RRÁ). Hægt er að lýsa þessu ferli í einfaldaðri mynd með sundrum á tvíatóma sameind

$$AB + e^- \longrightarrow AB^{-*} \longrightarrow A + B^-$$

þar sem innsend rafeind með litla orku er gripin af óhlaðinni sameind, AB, og myndar við það neikvæða jón í örvuðu titringsástandi (AB^{-*}) sem getur (a) kastað af sér rafeindinni eða (b) sundrast tvo hluta, óhlaðinn (A) og neikvætt hlaðinn (B^-). Þetta er eingöngu mögulegt ef orka kerfisins er hærri en orkuþröskuldur sundrunarinnar.

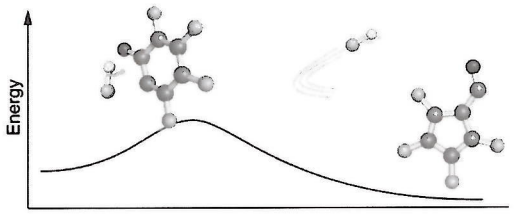
Þegar sameind grípur lágorkurafeind má líta á ferlið útfrá stöðuorkuyfirborði kerfisins fyrir og eftir atburðinn sem lóðrétta tilfærslu á milli grunnástands sameindarinnar yfir í tiltekið ástand neikvæðu jónarinnar. Þessi tilfærsla er einungis möguleg á þröngu orkubili á Franck-Condon svæðinu. RRÁ ferli eru almennt séð mjög sértæk, ákveðin tengjarof eru háð orku rafeindarinnar, en þau hafa líka mjög há þversnið við lága rafeindaorku. Algeng þversnið fyrir RRÁ ferla nálægt 0 eV eru 10^{-16} til 10^{-18} m^2[1]. Það er því ekki langsótt að íhuga RRÁ með lágorkurafeindum sem aðferð til að ná stjórn á efnahvörfum á sameindaskala.

Til viðbótar við einföld RRÁ ferli, þar sem einingis eitt tengi er rofið, hafa flóknari hvörf sést sem er ekki hægt að lýsa útfrá sundrun á tvíatóma sameind. Slík ferli geta falið í sér töluverða umröðun á myndefnum en samt gerst við lága orku, haft mjög hátt þversnið og þó haldið í sértæknina sem einkennir RRÁ. Sem dæmi um slík ferli má nefna mælingar á tríflúoróediksýru [3] og pentaflúorófenýlasetónítríl [4].

Í báðum þessum rannsóknum myndaðist jónin $[M-HF]^-$ nálægt 0 eV, þar sem M táknar upphaflegu sameindina, hér er því um að ræða rof á tveimur efnatengjum. Myndun á HF er útvermin en bindiorka HF er $\approx$ 5.8 eV. Hér virkar HF myndunin því sem drifkraftur fyrir efnahvarf sem væri annars ómögulegt.

Á síðustu árum hefur oft verið litið til RRÁ sem aðferðar til að stjórna efnafræði á sameindaskala. Í því samhengi er mjög áhugavert að leita leiða til þess að nýta myndun á efnatengjum með háa bindiorku sem drifkraft fyrir annars ómöguleg hvörf.

Með þessar hugmyndir í huga hófum við kerfisbundnar athuganir, bæði með tilraunum og fræði, á RRÁ efna sem eru líkleg til að mynda HF í ferlinu. Við völdum perflúorófenýl efni með mismunandi sethópa, pentaflúóranilín (PFA); $C_6F_5NH_2$, pentaflúorófenól (PFP); C_6F_5OH og pentaflúorótólúen (PFT); $C_6F_5CH_3$. Vegna mismunandi skautunnar á sethópunum töldum við líklegt að mikinn mun mætti sjá frá RRÁ á milli PFA og PFP annars vegar og PFT hins vegar. Bæði PFA og PFP innihalda rafneikvæð atóm (N og O) sem eru meðal annars þekkt fyrir eiginleika sýna til að mynda vetnistengi. Innansameindarvetnistengi á milli F$\cdots$H-O annars vegar og F$\cdots$H-N hins vegar stöðga sameindina á þann hátt að HF myndun er auðveldari eftir að sameindin hefur gripið rafeind.



Mynd 1. Myndræn framsetning á HF myndunninni. Eftir að rafeindin sest á sameindina (C_6F_5OH) myndast HF sem kemur af stað umröðun á neikvæða sameindabrotinu.

Heimildir

[1] L. Christophorou, J. Olthoff *Appl. Surf. Sci.* (2002) **192** (1-4) 309

[2] Papp et al. *J Chem Phys* (2006) **125** 204301

[3] Langer et al. *Chem Phys Lett* (2006)**419** 228

[4] Dabkowska et al. *Phys. Chem. Chem. Phys.* (2009) **11** 5323

Poster 14

Bond formations and rearrangement reactions in DEA experiments

B. Ómarsson*, E. H. Bjarnason*, S. Haughey†, O. Ingólfsson*, T. A. Field†

*Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland
†School of Mathematics and Physics, Queen's University Belfast, Belfast BT7 1NN, Northern Ireland, UK

In the low energy regime, electron molecule interaction are governed by inelastic collisions known as resonant electron capture or electron attachment (EA). These processes can lead to dissociation of the molecule through Dissociative Electron Attachment (DEA). In a simplified picture many DEA processes can be fairly well described within the model of a quasi-diatomic dissociation by

$$AB + e^- \longrightarrow AB^{-*} \longrightarrow A + B^-$$

where the incoming electron attaches to a neutral molecule, AB, to form a transient negative ion (TNI), AB^{-*}. The TNI can reemit the attached electron via autodetachment or, if it is energetically above the threshold for dissociation, dissociate to form a neutral fragment, A, and a negative ion, B^-. Electron attachment can be seen as a resonant vertical transition from the neutral ground state to the TNI, which is only accessible for a narrow electron energy range in the Franck-Condon region. In general, DEA processes are very bond selective with regards to the incident electron energy and at low energies frequently exhibit large cross sections of about 10^{-16} to 10^{-18} m^2[1]. It is, thus, not farfetched to consider DEA by low energy electrons as a method of chemical control at the molecular level. More complicated DEA processes are observed, however, which cannot be described within the quasi-diatomic model. Such processes can involve substantial rearrangement within the fragments formed, but still proceed at very low energies, be very efficient and maintain the intrinsic selectivity of DEA. Notable examples of such a process are studies on perfluoronated compounds such as trifluoroacetic acid [3] and pentafluorophenylacetonitrile [4]. There the abstraction of a neutral HF (BDE $\approx$ 5.8 eV) molecule forming the parent less HF, $[M\text{-}HF]^-$, acts as a driving force for a dissociative channel that would otherwise be energetically unavailable.

In the context of chemical control through DEA it is, thus, very interesting to seek ways to exploit highly exothermic bond formation processes, such as the HF formation, as a driving force for dissociation channels that would otherwise not be accessible.

Motivated by this concept we have conducted a systematic experimental and theoretical study of DEA to the substituted pentafluorophenyl compounds pentafluorotoluene (PFT); $C_6F_5CH_3$, pentafluoroaniline (PFA); $C_6F_5NH_2$ and pentafluorophenol (PFP); C_6F_5OH. We have chosen these compounds as, from a steric point of view, they can all form HF between an H atom and a fluorine in the ortho-position but they differ with respect to the polarization of the X-H bonds, which increases in the order C < N < O. We expected a large difference between PFT on one hand and PFA and PFP on the other as the more electronegative N and O, like F, form hydrogen bonds that may stabilize XHF intermediates.

With the aid of quantum chemical calculations we discuss the energetically favoured rearrangement reactions. Furthermore we discuss the existence of intramolecular hydrogen bonds which aid the formation of HF from the TNI.

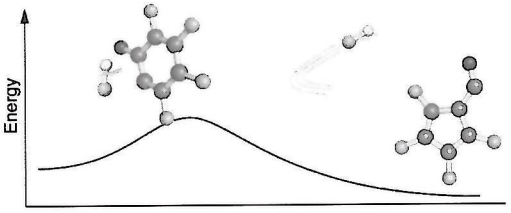


Figure 1. Graphical representation of the HF abstraction mechanism. After the electron attaches to the molecule (C_6F_5OH) HF is formed followed by rearrangement of the anionic fragment.

References

[1] L. Christophorou, J. Olthoff *Appl. Surf. Sci.* (2002) **192** (1-4)

[2] Papp et al. *J Chem Phys* (2006) **125**

[3] Langer et al. *Chem Phys Lett* (2006)**419**

[4] Dabkowska et al. *Phys. Chem. Chem. Phys.* (2009) **11**

Poster 15

More complex than expected: The self-interaction corrected ground state of atoms and molecules

Simon Klüpfel, Peter Klüpfel, Hannes Jónsson

Science Institute and Faculty of Science, VR-III, University of Iceland, Reykjavík, Iceland

Density functional theory (DFT) [1] has by now become the most widely used tool in calculations of chemical properties. In DFT, the exact ground-state of electronic systems can be calculated from the electron density alone and the ground-state energy also includes the contributions stemming from electronic correlation, which are missing in Hartree-Fock (HF). While this is true in theory, such a calculation would indirectly involve the solution of the many-body Schrödinger equation, which is in most cases not feasible. The common approach in modern DFT is to approximate the complicated terms in the energy expression, the exchange and correlation energy, by a simpler expression, E_{xc}, depending on the density alone (local density approximation, LDA) or also including dependencies on the gradient of the density (generalized gradient approximation, GGA).

For a given density of N electrons, the energy is evaluated using a fictitious system of N non-interacting electrons, φ^N, producing the same density:

$$E_{\mathrm{DFT}}[\rho] = T_{\mathrm{s}}[\varphi^N] + V[\rho] + E_{\mathrm{H}}[\rho] + E_{\mathrm{xc}}[\rho]$$

Here, $T_{\mathrm{s}}[\varphi^N]$ is the kinetic energy of this fictitious system, $E_{\mathrm{H}}[\rho]$ is the classical Coulomb repulsion of the electron density with itself, and $E_{\mathrm{xc}}[\rho]$ contains the exchange and correlation energy, which is usually approximated.

DFT significantly improves the total energy over Hartree-Fock (HF) and gives acceptable accuracy with smaller computational effort. However, the approximations in the exchange-correlation energy result in a problem: In HF, both the Coulomb repulsion energy as well as the exchange energy contain contributions from the interaction of each electron with itself, but they cancel exactly. In DFT, a spurious self-interaction energy of the electrons remains due to the approximation made. This is seen as the main reason for some of the failures of DFT: Bond energy tends to be too large while activation energy for atomic rearrangements tends to be underestimated. There is also a tendency to over delocalize spin density, sometimes making localized electronic defects unstable with respect to delocalization. Perdew and Zunger [2] proposed an orbital based self-interaction correction (SIC) which cures some of the problems of DFT, while worsening the results in other cases. In this formalism, the DFT energy is corrected by energy contributions, evaluated from the density of the single orbitals, ρ_i, with the same approximation of the exchange-correlation functional:

$$E_{\mathrm{SIC}}[\rho] = E_{\mathrm{DFT}}[\rho] - \sum_{i=1}^{N} (E_{\mathrm{H}}[\rho_i] + E_{\mathrm{xc}}[\rho_i])$$

Several systems had been studied in the last 30 years using this approximate correction. Recently, we calculated the ground state of atoms from hydrogen to argon using the Perdew-Zunger SIC to LDA and GGA functionals [3]. The correction can significantly improve the total energy, but we found that the true ground-state is only accessible, if the orbitals φ^N are allowed to be complex functions. If only real orbitals are considered, which is usually the case for HF and DFT calculations, a significantly higher ground-state energy is found for all but the smallest atoms. Previously, results using real orbitals had disqualified the SIC for use with GGA functionals, which is actually not the general case.

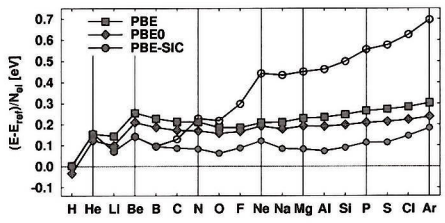


Figure 1. Errors in atomic total energy for GGA functionals of the PBE family. Empty symbols show results obtained with real orbitals.

This illustrates the importance of using complex orbitals for systems described by orbital density dependent energy functionals, of which the Perdew-Zunger SIC is only one example.

References

[1] W. Kohn, *Rev. Mod. Phys.* **71**, 1253 (1999).

[2] J.P. Perdew and A. Zunger, *Phys. Rev. B* **23**, 5048 (1981).

[3] S. Klüpfel, P. Klüpfel and H. Jónsson, *Phys. Rev.* A **84**, 050501 (2011).

Poster 16

Localized electrons at the surface of TiO_2

Hildur Gudmundsdóttir, Peter Klüpfel and Hannes Jónsson

Science Institute and Faculty of Science, University of Iceland, VR-III, 107 Reykjavík, Iceland

Metal oxide surfaces play an important role in chemical catalysis. TiO_2 has been studied extensively and is, for example, a promising material for solar cells producing hydrogen. Oxygen vacancies are typically abundant on oxide surfaces and are believed to play a role in various catalytic processes as well as nucleation of metal cluster growth. Experiments indicate that electrons are localized near the vacancy and are associated with defect states with energy ca. 0.8 eV below the conduction band edge[1].

Theoretical calculations can help interpret experimental data and guide searches for new and improved materials. The commonly used methodology for calculating electronic properties of solids, density functional theory (DFT) with gradient dependent functionals such as PBE, however often fails to describe electronic defects. The oxygen vacancy on the surface of TiO_2 [2] is one example. Furthermore, this level of theory is not able to predict the band gap of solids, a quantity of particular interest in the design of solar cells.

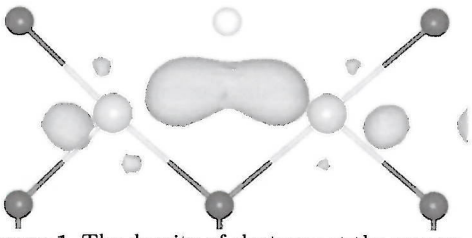


Figure 1. The density of electrons at the oxygen vacancy at $TiO_2(110)$ (indicated with fictitious white sphere).

In order to improve the accuracy of the theoretical calculations and make it possible, in particular, to study band gaps and defect states in oxides, we have implemented recently developed methodology [3] for using scaled Perdew-Zunger self-interaction correction (SIC) [4] to density functionals in the real-space grid code GPAW. There, the total energy is

$$E_{\mathrm{SIC}}[\{n_i\}] = E_{\mathrm{DFT}}[n] - \alpha \sum_i \left(E_{\mathrm{H}}[n_i] + E_{\mathrm{xc}}[n_i]\right)$$

where $\alpha = 1/2$ is a universal scaling factor. Within this formalism, the total energy is orbital-density dependent and the numerical methods used in conventional DFT are no longer applicable [3]. This methodology has been applied to atoms, molecules and extended systems. Here, we present results of calculations performed on the rutile (110) surface of TiO_2.

The TiO_2 surface has been modeled with scaled PBE-SIC (PBE-SIC/2), as well as the conventional PBE functional for comparison. The PBE-SIC/2 results show that two electrons are localized at the site of the vacancy and they have spin in the same direction, i.e. a triplet state. Two orbital energies are associated with this defect state, with a shift down from the conduction band that is consistent with experimental measurements. The predicted band gap is 3.7 eV as compared with the experimental estimate of 3.0 eV. The standard methodology, DFT/PBE, however, gives much too small a band gap, 1.7 eV, the defect states are much closer to the conduction band for PBE, and the spin density indicates that these states are quite delocalized, a common problem with this level of theory. An important issue is the chemical reactivity of such localized electrons on the surface and with the new theoretical development, the stage is set for such studies.

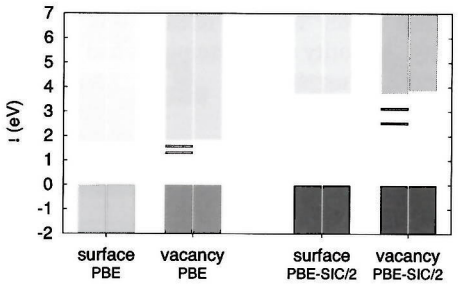


Figure 2. Orbital eigenvalues found from PBE and PBE-SIC/2 calculations of the $TiO_2(110)$ surface with and without an oxygen vacancy.

References

[1] U. Diebold, *Surface Science Reports* **48**, 53 (2003).

[2] Di Valentin, Pacchioni and Selloni, *Phys. Rev. Lett.* **97**, 166803 (2006).

[3] P. Klüpfel, S. Klüpfel, H. Jónsson and K. Tsemekhman, *Lecture Notes in Computer Science* (in print); P. Klüpfel, S. Klüpfel, and H. Jónsson, *Phys. Rev. A Rapid Communication* **80**, 050501 (2011).

[4] J. P. Perdew and A. Zunger, *Phys. Rev. B* **23**, 5048 (1981).

Poster 17

Experimental Design for the Optimization of Silicone Drug Delivery Matrix

Másson, M.[1], Snorradóttir, B.S.[1], Thorsteinsson, F.[2], and Guðnason, P.I.[2]

[1]Faculty of Pharmaceutical Sciences, University of Iceland, Reykjavik, Iceland.
[2]Össur hf., Reykjavik, Iceland.

As a continuation of our previous work [1] with silicone and NSAIDs, we have applied experimental design software (MODDE) to optimize the material properties of silicone drug delivery matrix. The matrix contained drug particles and various excipients in different compositions. The aim was to engineer the elastomer material to provide excellent mechanical strength and optimal transdermal delivery.

The experimental design software proposed a D-optimal design for this system since the region becomes an irregular polyhedron. D-optimal designs are computer generated designs, tailor made for each problem [2]. They allow great flexibility in the specifications of each problem and are particularly useful when you want to constrain a region and no classical design exists.

The model was fitted with MLR (multiple linear regression), which gave a G-efficiency of 73.5%. Evaluation of the raw data replication plot suggests a reasonably good model. The coefficient plots showed correlation (Q^2 >0.5) of the excipients on all of the responses, and the most important factor for the release was the drug quantity. Majority of the excipients had a positive influence on the release.

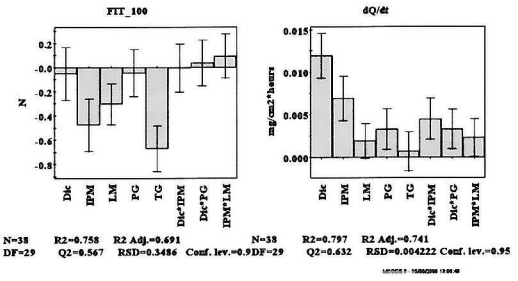


Fig. 1 Coefficient plots for the responses FIT_100 (on the left) and dQ/dt (on the right) with confidence intervals (error bars). The plots are analogous for FIT_100 and FIT_200 on one hand and for Rel_1, Rel_2 and dQ/dt on the other hand.

In vitro transdermal permeation studies were done with 9 compositions of the drug delivery matrix that were proposed as optimal by MODDE. Human skin from 3 Caucasian female patients was obtained from cosmetic surgery and used to perform the drug release studies through the skin barrier. Diffusion experiments were done with heat separated dermis and epidermis from full thickness skin.

Table 1 lists optimized values for all of the factors as well as criteria and limits for the optimization and predicted results from optimization. Log(D) number determines the "best" optimization (the lowest log(D) value by MODDE).

Responses	Criteria	Min - Target *	Min - Target - Max **	Predicted results from optimization	
FIT_100	Max * Target **	2.009-2.221	1.2 - 1.7 - 3.0	1.714 *	1.285 **
FIT_200	Max * Target **	3.152-3.483	2.0 - 2.5 - 4.0	2.622 *	1.993 **
Rel_1	Max	0.251-0.275	0.251 - 0.275 - NL	0.225 *	0.243 **
Rel_2	Max	0.311-0.340	0.311 - 0.340 - NL	0.280 *	0.301 **
dQ/dt	Max	0.028-0.031	0.028 - 0.031 - NL	0.026 *	0.027 **

Optimized values for the factors (NL – not listed).
* Na-diclo: 0.05 - IPM: 0.02 - PG: 0.08 (LM and TG: 0). Log(D) = 0.70
** Na-diclo: 0.05 - IPM: 0.06 - PG: 0.04 (LM and TG: 0). Log(D) = 0.15

The transdermal transport increased when the silicone matrix contained enhancers. . As can be expected there was considerable experimental variation in tests using human skin samples but the difference between the proposed optimized silicone membrane (6% IPM – 4% PG) and silicone without enhancer was statistically significant. Since the drug release from the silicone is a limiting factor the influence of the enhancers on the skin is not as explicit as we would like it to be. Although the enhancers may have some effect to improve transdermal transport the effect on release from the silicone matrix is much greater.

References

1. Snorradottir, B.S., et al., *Release of anti-inflammatory drugs from a silicone elastomer matrix system.* Pharmazie, 2009. **64**(1): p. 19-25.
2. Eriksson, L., et al., *Design of Experiments, Principles and Applications*. 2000, Stockholm: Learnways AB.

Poster 18

Synthesis of tert-butyldimethylsilyl Chitosan and Application in Superhydrophobic Biomimetic Films

Már Másson[1], Vivek Gaware[1], Berglind E. Benediktsdóttir[1], Wenlong Song[2] and Joao F. Mano[2],

[1]University of Iceland, Hagi, Hofsvallagata 53, IS-107 Reykjavik, Iceland, [2] IBB, PT Government Associated Laboratory, Guimaraes, Portuga

Chitosan and chitosan derivatives have been used in the fields of biomedicine, biomembranes and food/nutrition because of their biocompatible properties. However, water solubility of chitosan at pH < 5 strongly limits the use of chitosan-based films when pH stability and low water uptake are required in many actual applications.

Recently we have demonstrated that the di-3,6-O-*tert*-butyldimethylsilyl-chitosan is a useful precursor for synthesis that has excellent solubility in organic solvents and is extreme hydrophobic[1].

Objective: Aim of the current work was to optimize the reaction conditions for the synthesis of TBDMS-chitosan which is useful starting material to prepare extreme water-repellent films in the whole pH range 1 to 14 that exhibit topography with a three level hierarchical roughness organization.

Results: In the original protocol, chitosan polymer mesylate salt was reacted with 10 fold excess TBDMSCl in DMSO to obtain full silylation of the 6-O and 3-O hydroxyl groups. However it was difficult to reproduce or improve this procedure. Initial investigation different reaction conditions commonly yielded material that was only partially silylated and therefore poorly soluble in organic solvent. A key step in a improved procedure was recrystallization of the mesylate salt and with this starting material it was possible to fully O-silylate chitosan with 2.5 fold excess of TBDMSCl and reduced reaction time. The peaks for the sugar backbone were then fully resolved in H-1 NMR spectra ($CDCl_3$). Two peaks of equal intensity at 0.890 and 0.903 ppm for the *tert*-butyl groups and four peaks at 0.047, 0.06, 0.099, 0.125 ppm for the methyl groups, were observed (Fig.1). These results clearly demonstrated that there was 100% substitution of the hydroxyl groups and this was also confirmed by IR.

The fully silylated compound used to prepare extreme water-repellent films in the whole pH range 1 to 14 using a phase separation method that exhibit topography with a three level hierarchical roughness organization[2] (Fig. 2). The polymer also allows chemical modification specifically through the amine group, permitting to control the surface chemistry and wettability. Chitosan-based films with improved stability were produced the possibility of manufacturing polysaccharide-based superhydrophobic surfaces with potential to be used in antibacterial substrates, tissue engineering, food industry and other biomedical applications, was also demonstrated.

Conclusions: In conclusion, the synthesis method of 3,6-O-di-tertbutyldimethyl silyl chitosan (SC) was improved and this polymer was used to prepare durable superhydrophobic films using a simple and low-cost phase separation method. These materials could find applications in anti-bacterial or impermeable textiles, tissue engineering and other biomedical applications, or membrane technology.

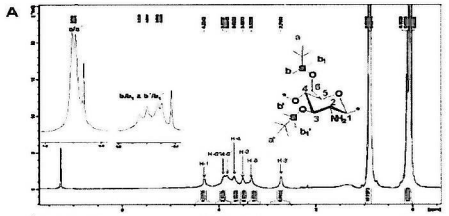


Fig. 1 ^{1}H NMR spectrum ($CDCl_3$) and structure of di-*tert*-butyldimethyl chitosa

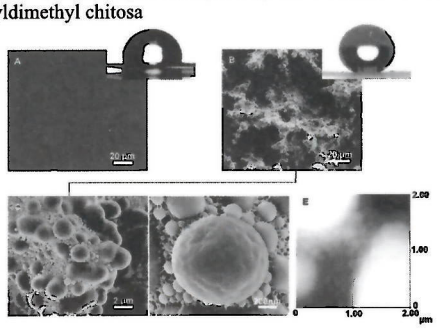


Fig. 2 A and B: representative SEM images of smooth and rough chitosan film (obtained using a 50 mg/ml SC solution); on the top right corner of these micrographs, the profiles of the water drops deposited onto the films are shown, with CAs of 103.6±2.7^0 and 151.5±1.9^0, respectively. C and D: magnified images of the superhydrophobic surface, which displayed abundant number of micro and nano particles. E - AFM image on the superhydrophobic surface.

References

1. Runarsson O. V., Malainer C., Holappa J., Sigurdsson S. Th., & Masson M., Carbohydrate Research 2008, **343**, 2576-2582

2. Song W., Gaware V. S., Runarsson O. V., Masson M., Mano J., *Carbohydrate Polymer* 2010, **81** (1) 140-144

Poster 19

Selective synthesis of *N,N,N*-trimethyl chitosan homopolymer and *N*-alkyl-*N,N*-dimethyl-chitosan

Már Másson[1], Berglind E. Benediktsdóttir[1], Vivek S. Gaware[1], and Knud J. Jenssen[2]

[1]Faculty of Pharmaceutical Sciences, University of Iceland, Reykjavik, Iceland., [2]Faculty of Life Sciences, University of Copenhagen, Copenhagen, Denmark

As a continuation of our previous work [1] with Chitosan (poly-β-(1-4)-glucosamine, Figure 1) is a biopolymer, derived from chitin, with many potential nanomedical application of which enhanced paracellular transport of drugs is of special interest [1,2]. The major limitation of this polymer is poor aqueous solubility at physiological pH, limiting the applicability for *in vitro/in vivo* testing. Furthermore, poor solubility in organic solvents is a limiting factor for synthesis of new nanomaterials derived from chitosan. Currently used procedures can also lack selectivity and the product of such reaction can therefore be rather poorly defined.

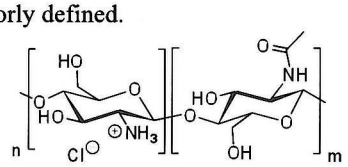


Figure 1 Chitosan is composed of glucosamine (left) and *N*-acetyl glucosamine (right) units.

Aim Selectively *O*-protect chitosan by reaction with tert-butyldimethylsilyl (TBDMS) chloride and use the protected chitosan for synthesis of quaternized chitosan derivatives such as *N,N,N*-trimethyl chitosan (figure 2.A) and different *N*-alkyl-*N,N*-dimethyl chitosan (figure 2.B).

Results Chitosan polymer could be converted to the DMSO soluble mesylate salt which was then reacted with TBDMSCl in DMSO, yielding fully *O*-protected chitosan that had unprecedented solubility in organic solvents. This 3,6-*O*-di TBDMS chitosan, solubilized in CH_2Cl_2, was reacted with alkyl aldehydes of different chain lengths giving *N*-alkyl-imine TBDMS chitosans with around 0.70 degree of N-substitution according to ^{1}H-NMR which showed distinct imine proton peak at 7,44 ppm. The imine was reduced with borohydride yielding mono-*N*-alkyl TBDMS chitosan confirmed by COSY NMR and the disappearance of the imine proton peak.

The *N*-alkylated TBDMS chitosan was then quaternized with dimethyl sulfate (DMS) as methylating agent and deprotected with tetrabutylammonium fluoride (TBAF) yielding quaternized *N*-alkyl- *N,N*-dimethyl chitosan with a distinct dimethyl peak at 3,28 ppm for *N*-propyl-*N,N*-dimethyl chitosan and 3,29 ppm for *N*-hexyl-*N,N*-dimethyl chitosan. Distinct peaks for the *N*-mono- and *N,N,N*-trimethylated derivatives were also observed by ^{1}H NMR. Interestingly, when the TBDMS chitosan was quaternized directly with MeI and deprotected with TBAF it resultet in a fully quaternized *N,N,N*-trimethyl chitosan with a characteristic trimethyl peak at 3.365 ppm and no *O*-methylation or dimethylation peak.

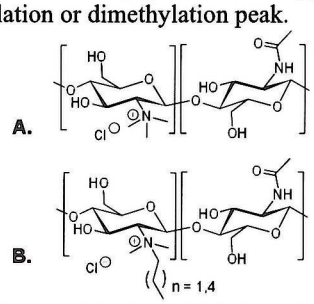


Figure 2 Chitosan derivatives *N,N,N*-trimethyl chitosan (A) and *N*-alkyl-*N,N*-dimethyl chitosan (B).

Discussion. TBDMS chitosan could be fully trimethylated but full quaternization of *N*-alkyl-*N,N* dimethyl chitosan was not achieved which could be explained by steric hindrance due to the bulky TBDMS group neighboring the *N*-alkyl chain, reducing reactivity and thus preventing full conversion. This conclusion was also supported by the fact that MeI did not quaternize the *N*-alkylated polymer but needed a much stronger methylating agent in the form of DMS to quaternize the chitosan. Furthermore, the reaction only proceeded when heated suggesting that the steric hindrance played an important role in the reaction.

These results clearly indicate that TBDMS-*O*-protected chitosan is a useful precursor for *N*-selective modification of chitosan such as *N*-alkylation and quaternization. However more vigorous conditions are required than normally used for the modification of amino groups.

Conclusion Synthesis of well defined quaternized chitosan derivatives was achived. This enables detailed studies of structure activity relationships and opens opportunities for investigation of these nanomaterials to overcome the biological barriers in pulmonary delivery of large peptides and proteins.

References

1. Mei, D.; Mao, S.; Sun, W.; Wang, Y.; Kissel, T. , *Eur, J. Pharm. Biopharm.* **2008,** *70* 874 – 881
2. Dodane, V.; Khan, M.A.; Merwin, J.R., *Int. J. Pharm.* **1999**, 182 21 - 32

Veggspjald 20

Olíuframleiðsla úr þörungum fóðruðum á útblástursgasi jarðvarmavirkjana

Olof K. Hrafnsdottir[1], Asa Brynjolfsdottir[2], Halldor G. Svavarsson[1,2*]

[1]Reykjavik University, School of Science and Engineering, [2]Blue Lagoon ltd, *Corresponding author: *halldorsv@ru.is*

Þörungar, ræktaðir við Bláa Lónið hf, eru notaðir sem hráefni í ýmsar snyrtivörur fyrirtækisins. Önnur notkun þeirra, svo sem í fiskafóður og eldsneyti gæti orðið raunhæfur möguleiki í náinni framtíð. Líkt og plöntur, breyta þörungar CO_2 í lífmassa með aðstoð ljósorku. Sumar þörungategundir geta innihaldið allt að 40% þurrmassa sem olíu. Markmið þessa verkefnis var að rækta, með útblástursgasi jarð-varmavera, þörunga með háu fituinnihaldi. Þörungategundin Apmhiprora var valin til ræktunar þar sem fyrri rannóknir Bláa Lónsins hf höfðu bent til þess að sú tegund gæti gefið hátt fituhlutfall. Áhrif sýrustigs, hitastigs, hrærslu og næringarstigs voru könnuð. Sýnt var fram á að sveltiástand þörunganna skilaðu hæsta fitu-hlutfallinu. Þörungar með yfir 20% fituhlutfall voru ræktaðir

Oil production from algae fed on geothermal flue gas

Olof K. Hrafnsdottir[1], Asa Brynjolfsdottir[2], Halldor G. Svavarsson[1,2*]

[1]Reykjavik University, School of Science and Engineering, [2]Blue Lagoon ltd, *Corresponding author: *halldorsv@ru.is*

Algae, cultivated at the Blue Lagoon ltd, are currently being used as an active ingredient in the Blue Lagoon's skin care products. Other applications such as for animal feed and bio-fuel may become relevant in the near future. Like plants, algae convert CO_2 to biomass with photosynthesis. Depending on the species, algae may contain up to 40% wt lipid. Until now, the algae have been fed on commercially available CO_2. In this work the objective was to cultivate algae, fed on geothermal CO_2 flue gas, with high lipid content. The algae species Amphiprora was chosen since earlier research, carried out at the Blue Lagoon ltd, indicated it could be a powerful lipid producer. The effect of pH value, temperature, ventilation and nutrition level was investigated. It was observed that starving condition at high pH level gave the highest ratio of lipid. Algae with lipid content in excess of 20% wt were cultivated.

Veggspjald 21

Áhrif n-3 fjölómettaðra fitusýra í fóðri á lípíðasamsetningu og staðsetningu próteina í himnuflekum úr rottuhjarta

Jón Otti Sigurðsson*, Guðrún Skúladóttir#,Ingibjörg Harðardóttir †, Bjarni Ásgeirsson* og Valgerður Edda Benediktsdóttir*.

*Raunvísindastofnun, Verk- og Náttúruvísindasviði Háskóla Íslands, Dunhaga 3, 107 Reykjavík.
#Lífeðlisfræðistofnun, †Lífefna- og sameindalíffræðistofa, Læknadeild, Heilbrigðisvísindasviði Háskóla Íslands, Vatnsmýrarvegi 16, 101 Reykjavík.

Staðsetning próteina í himnuflekum í frumuhimnu hjartavöðvafruma er mikilvæg fyrir boðflutninga, en himnuflekar eru örsvæði á frumuhimnu, sem eru stífari og innihalda meira kólesteról og sphingólípíð en himnan umhverfis. Lækkuð dánartíðni vegna hjartasjúkdóma hefur tengst neyslu n-3 fjölómettaðra fitusýra (FÓFS), en þær eru taldar vernda gegn hjartsláttartruflunum, hugsanlega með því að hafa áhrif á boðflutning í hjartavöðvafrumum. Áður hefur verið sýnt að n-3 FÓFS hafa áhrif á staðsetningu próteina í himnuflekum og á lípíðasamsetningu þeirra í eitilfrumum og fleiri frumugerðum.[1,2,3] Áhrif n-3 FÓFS á staðsetningu próteina í himnuflekum í hjartavöðvafrumum hafa ekki verið könnuð.

Markmið þessa verkefnisins var að kanna áhrif þeirra á lípíðasamsetningu himnufleka og staðsetningu próteina í himnuflekum í rottuhjörtum.

Himnuflekar voru einangraðir með spuna á sykurstyrkhalla úr hjarta fullorðinna rotta sem aldar voru á fóðri bættu með fiskolíu (n-3 FÓFS) eða körfublómaolíu (n-6 FÓFS). Prótein og voru greind í 12 hlutum af styrkhallanum með western þerrun, gangliosíð GM1 með þerriblettun og kólesteról var mælt með ljósmælingu. Caveolin 3, flotillin 1, GM1 og kólesteról, sem öll einkenna himnufleka, einangruðust í hlutum nr. 4, 5 og 6, talið ofanfrá á sykurstyrkhallanum og voru þessir hlutar skilgreindir sem himnuflekar. Fosfólípíð voru einangruð úr himnuflekum og fitusýrusamsetning þeirra var greind með gasgreini.

Frumniðurstöður úr verkefninu sýna að meira var af n-3 FÓFS í fosfólípíðum himnufleka úr hjörtum dýra sem fengu fiskolíu en þeirra sem fengu körfublómaolíu. Ekki var munur á styrk kólesteróls í himnuflekum úr hjörtum dýra sem fengu mismunandi fóður. $Alfa_1$ adrenergir viðtakar voru að mestu í himnuflekum, en $beta_1$ adrenergir viðtakar fundust bæði í himnuflekum og í himnum utan þeirra, í samræmi við það sem aðrir hafa fundið í hjartavöðvafrumum. Fyrstu niðurstöður sýndu ekki mun milli fóðurhópa á magni þessara viðtaka í himnuflekum.

Niðurstaða: Einangraðir voru himnuflekar úr hjörtum rotta sem aldar voru á fóðri bættu með n-3 eða n-6 FÓFS. N-3 FÓFS úr fóðri dýranna komu fram í fosfólípíðum himnuflekanna. Samkvæmt frumniðurstöðum rannsóknarinnar sást þó ekki munur milli fóðurhópa á kólesteróli né gangliosíð GM1 magni, og ekki heldur á staðsetningu $alfa_1$- og $beta_1$ adrenergra viðtaka í himnuflekum.

Tilvitnanir

[1] Schley PD, Brindley DN, Field CJ. (n-3) PUFA alter lipid composition and decrease epidermal growth factor receptor levels in lipid rafts of human breast cancer cells. *J Nutr* **137**:548-553, 2007.

[2] Fan YY, LY LH, Barhoumi R, Amcamurray DN, Chapkin RS. Dietary docosahexaenoic acid suppresses T-cell protein kinase C theta lipid raft recruitment and IL-2 production. *J Immunol* **173**: 6151-61. 2004.

[3] Li Q, Ma J, Tan L, Wang C, Li N, Xu G, Li J. Effect of docosahexaenoic acid on interleukin-2 receptor signaling pathway in lipid rafts. *Sci China C Life Sci* **49**:63-72. 2006.

Poster 21

The Effect of Dietary n-3 Polyunsaturated Fatty Acids on Lipid Composition and Location of Proteins in rat heart lipid rafts

Jón Otti Sigurðsson*, Guðrún Skúladóttir[#], Ingibjörg Harðardóttir[†], Bjarni Ásgeirsson* og Valgerður Edda Benediktsdóttir*.

*Science Institute, School of Engineering and Natural Sciences, Dunhaga 3, IS-107 Reykjavík.
[#]Dept. of Physiology, [†] Department of Biochemistry and Molecular Biology, Faculty of Medicine, School of Health Sciences, University of Iceland, Vatnsmyrarvegur 16, IS-101 Reykjavik, Iceland.

Location of proteins in lipid rafts in cardiomyocyte membranes is important for transmembrane signaling as they serve as a platform for signaling across membranes. Lipid rafts are microdomains in the cell membrane that have higher concentration of cholesterol and sphingolipids and are more tightly packed than the surrounding membrane. N-3 polyunsaturated fatty acids (PUFA) in diet have been shown to lower the risk of cardiovascular diseases, potentially by affecting signal transduction across the cardiomyocyte membrane. Studies have shown that n-3 PUFA alter location of proteins in lipid rafts and their lipid composition in T-cells and other cell types.[1,2,3] The effect of n-3 PUFA on location of proteins in lipid rafts in cardiomyocytes has not been investigated. The aim of this project was to study the effect of dietary n-3 PUFA on the lipid composition and the location of adrenergic receptors in lipid rafts in rat heart. Lipid rafts were isolated on sucrose gradient from a hearts of adult rats that had been fed a controlled diet enriched with fish oil (n-3 PUFA) or safflower oil (n-6 PUFA). Proteins and GM1 gangliosid were analyzed in 12 fractions of the sucrose gradient with western blot and dot blot technique, respectively. Cholesterol was measured with spectrophotometric assay kit. Caveolin 3, flotlilin, GM1 and cholesterol, which characterize lipid rafts, were isolated in fractions 4, 5 and 6, counted from the top of the sucrose gradient and those fractions were assumed to be lipid rafts. Phospholipids were isolated from lipid rafts and their fatty acid composition of phospholipids was analyzed with gas chromatography.

Preliminary results showed that the n-3 PUFA level was higher in phospholipids of lipid rafts from rats fed fish oil than rats fed safflower oil but the amount of cholesterol was similar in both diet groups. Alpha 1 adrenergic receptor was located mostly in lipid rafts, but Beta 1 adrenergic receptor was found in both lipid rafts and soluble fractions. Preliminary results did not show difference in the location of the receptors in lipid rafts, between diet groups.

Conlusion: Lipid rafts were isolated from hearts of rats fed diets enriched with n-3 or n-6 PUFA. N-3 PUFA levels were higher in the lipid rafts from rats fed n-3 PUFA than those fed n-6 PUFA. Preliminary results showed no significant difference in cholesterol levels, GM1 or protein location in lipid rafts between the n-3 and n-6 PUFA fed rats.

References

[1] Schley PD, Brindley DN, Field CJ. (n-3) PUFA alter lipid composition and decrease epidermal growth factor receptor levels in lipid rafts of human breast cancer cells. *J Nutr* **137**:548-553, 2007.

[2] Fan YY, LY LH, Barhoumi R, Amcamurray DN, Chapkin RS. Dietary docosahexaenoic acid suppresses T-cell protein kinase C theta lipid raft recruitment and IL-2 production. *J Immunol* **173**: 6151-61. 2004.

[3] Li Q, Ma J, Tan L, Wang C, Li N, Xu G, Li J. Effect of docosahexaenoic acid on interleukin-2 receptor signaling pathway in lipid rafts. *Sci China C Life Sci* **49**:63-72. 2006.

Veggspjald 22

Samanburður á tjáningu trypsíns-1 í tveimur kuldaaðlöguðum tjáningarkerfum.

Karen Ósk Pétursdóttir[1,2], Ágústa Guðmundsdóttir[1,3], Bjarki Stefánsson[1] og Hilmar Hilmarsson[1]. Netföng: ag@hi.is, bjarkis@hi.is, hilmarh@hi.is, kop1@hi.is

[1] Lífefnafræðistofa Raunvísindastofnunar Háskólans, Dunhaga 3-5, 107 R.
[2] Raunvísindadeild, Verkfræði- og Náttúruvísindasvið Háskóla Íslands.
[3] Matvæla- og næringarfræðideild, Heilbrigðisvísndasvið Háskóla Íslands.

Markmið þessa MS verkefnis er þríþætt. Í fyrsta lagi framleiðsla þorskatrypsíns í nýju kuldaaðlöguðu *Pseudoalteromonas haloplanktis* (*P. haloplanktis*) tjáningarkerfi í samstarfi við háskólann í Napoli á Ítalíu. Í öðru lagi að framleiða trypsín í nýju kuldaaðlöguðu *Escherichia coli* (*E. coli*) tjáningarkerfi. Í þriðja lagi að framleiða stökkbreytt afbrigði trypsíns-1 með aukinn stöðugleika gagnvart sjálfmeltu í því tjáningarkerfi sem best hentar. Verkefnið er hluti af PenXpressZyme verkefninu sem styrkt er af Tækniþróunar-sjóði.

Einkaleyfisvarða Pensímtæknin felur í sér notkun trypsína úr þorski í snyrtivörur, lækningatæki og lyf. PenXpressZyme verkefnið mun þróa og framleiða tjáð afbrigði þorskatrypsína og endurbættar afleiður þeirra. Sem lífvirkar sameindir munu tjáðu trypsínin mæta markaðslegri þörf fyrir ný lyf við psoriasis og exemi. Klínískar athuganir hafa sýnt jákvæð áhrif Pensím afurða á ofangreinda sjúkdóma.

Á fyrri hluta fyrsta árs MS verkefnisins var hafinn undirbúningur og aðferðir þróaðar. Einnig voru prófuð mismunandi bakteríuæti og ræktunarhitastig. Niðurstöðurnar sýndu að hámarkstjáning trypsíns-1 fékkst við 15°C í *E. coli* kerfinu en við 10°C í *P. haloplanktis* tjáningarkerfinu.

Á síðari hluta fyrsta styrkárs var hafin tjáning trypsíns-1 í ofangreindum tjáningarkerfum. Niðurstöður sýndu að tjáning í *P. haloplanktis* tjáningarkerfinu gaf af sér trypsín-1 með hærri virkni en *E. coli* kerfið.

Á fyrri hluta annars styrkárs hefur verið haldið áfram með þróun og uppskölun á framleiðslu trypsíns-1 í báðum tjáningarkerfunum en ljóst er að *P. haloplanktis* kerfið hentar betur til framleiðslu trypsíns-1 í miklu magni.

Á síðari hluta annars styrkárs verður unnið að þróun á stökkbreyttum afbrigðum trypsíns-1 sem hafa aukinn stöðugleika gagnvart sjálfmeltu. Þorskslóg verður áfram mikilvægur forði fyrir einangrun trypsína til notkunar í náttúruvörur. Tjáðu afbrigðin henta hins vegar almennt betur til að uppfylla lyfjastaðla. Þau munu einnig verða stöðugt forðabúr fyrir framleiðslu Pensím afurða. Í framtíðinni verða öll tækifæri sem Pensím tæknin felur í sér nýtt á sviði snyrtivara og lyfja í nánu samstarfi við alþjóðleg lyfjafyrirtæki.

Niðurstöður þessa verkefnis munu leiða til útskriftar MS nema árið 2012 og birtingar á grein í viðurkenndu erlendu vísindariti.

Poster 22

Comparison of trypsin-1 expression in two cold-adapted expression systems.

Karen Ósk Pétursdóttir[1,2], Ágústa Guðmundsdóttir[1,3], Bjarki Stefánsson[1] and Hilmar Hilmarsson[1]. Emails: ag@hi.is, bjarkis@hi.is, hilmarh@hi.is, kop1@hi.is

[1] Department of Biochemistry, Science Institute, University of Iceland, Dunhagi 3-5, 107 R.
[2] Faculty of Physical Sciences, School of Engineering and Natural Sciences, University of Iceland.
[3]Faculty of Food Science and Nutrition, School of Health Sciences, University of Iceland.

The goal of this MS project is threefold. Firstly, the production of cod trypsin in a new, cold-adapted *Pseudoalteromonas haloplanktis* (*P. haloplanktis*) expression system in cooperation with the University of Naples. Secondly, the production of trypsin in a new, cold-adapted *Escherichia coli* (*E. coli*) expression system. Thirdly, the production of mutated variations of trypsin-1 with a greater stability against autolysis in the expression system which proves to be more suitable. The project is a part of the PenXpressZyme project, which is sponsored by the Icelandic Centre for Research (Tækniþróunarsjóður).

The patented Penzyme Technology involves the use of cod trypsins as cosmetics and therapeutics. The PenXpressZyme project will develop and produce recombinant cod trypsins and stabilized derivates thereof. As a pharmaceutical, recombinant trypsins will meet a market demand for new psoriasis and eczema treatments. Clinical observations show positive effects of Penzyme for these diseases.

In the first part of the first year of the MS project, preparations were made and methodology developed. Also, different temperatures and bacterial growth media were tested. The results showed optimal trypsin-1 expression at 15°C with *E. coli* and at 10°C with *P. haloplanktis*.

In the latter part of the first year, expression of trypsin-1 commenced in the expression systems described. The results showed that expression with the *P. haloplanktis* system gave a more active trypsin-1 than that with *E. coli*.

In the first part of the second year, development and scale-up of trypsin-1 was continued in both expression systems. Clearly, *P. haloplanktis* is better suited for trypsin-1 production on a larger scale.

In the latter part of the second year, development of mutated varieties of trypsin-1 will take place, which will have a greater stability toward autolysis. Cod offal will remain an important resource for the isolation of trypsins for application in natural products. The expressed varieties, however, are generally better suited to meet medical standards. They will be a stable resource for Penzim products as well. A future goal is to realize all the potential of the Penzyme technology in the area of cosmetics and medicines in a close cooperation with international pharmaceutical companies.

The results of this research project will lead to the graduation of an MS student in 2012 and a publication in a peer-reviewed scientific journal.

Veggspjald 23

Samanburður á notkun þorskatrypsín afbrigða við niðurbrot próteina í svipmótaðri myndbyggingu

Guðrún Birna Jakobsdóttir[1,2], Ágústa Guðmundsdóttir[2,3], Bjarki Stefánsson[1] og Hilmar Hilmarsson[1]

[1]Lífefnafræðistofa Raunvísidnastofnunar Háskólans, Dunhaga 3-5 107 Rvk.
[2]Raunvísindadeild, Verkfræði- og náttúruvísindasviðs Háskóla Íslands
[3]Matvæla- og næringarfræðideild, Heilbrigðisvísindasviðs Háskóla Íslands

Markmið þessa MS verkefnis er tvíþætt. Í fyrsta lagi að rannsaka niðurbrot svipmótaðra próteina með blöndu þorskatrypsína í samanburði við nautatrypsín. Í öðru lagi að rannsaka niðurbrot svipmótaðra próteina, sem tengjast sáravessa, með þorskatrypsín blöndum og aðgreindum afbrigðum þeirra.

Verkefnið tengist verkefninu Örveruhemjandi eiginleikar SaliZyme nefskols, sem styrkt er af AVS rannsóknasjóði í sjávarútvegi.

Trypsín eru serín próteinkljúfar í meltingarvegi sem vatnsrjúfa prótein C-enda megin við amínósýrurnar lýsín og arginín í fjölpeptíðkeðju. Vitað er að próteinkljúfandi ensím flýta fyrir græðingu sára með niðurbroti próteina í sáravessa (e. wound exudate) [1]. Klínískar rannsóknir á notkun þorskatrypsína í vatnsgels blöndum við græðingu sára hafa gefið jákvæðar niðurstöður [2].

Á fyrri hluta fyrsta árs var verkefnið undirbúið og aðferðafræði þróuð. Á síðari hluta fyrsta árs var gerður samanburður á niðurbrotsmynstrum mismunandi próteina í náttúrulegri myndbyggingu með þorskatrypsíni annarsvegar og nautatrypsíni hinsvegar.

Rannsóknirnar voru gerðar við 4°C, 25°C og 37°C og niðurbrotið skoðað með HPLC tækni á mismunandi tímapunktum.

Niðurstöður gefa skýrt til kynna meiri getu trypsíns við að brjóta niður svipmótuð prótein miðað við nautatrypsín.

Einnig voru niðurbrotsafurðir greindar á rafdráttargeljum. Á fyrri hluta annars árs hafa mismunandi afbrigði þorskatrypsíns verið aðgreind úr þorskatrypsín blöndu á MonoQ jónaskiptasúlu. Til að nægilegt magn þroskatrypsín afbrigða fengist til rannsóknanna var þorskatrypsín blanda hreinsuð á *p*-aminobenzamidine súlu úr 15 L af ensím útdrætti úr skúflöngum þorsks (*Gadus morhua*).

Á síðari hluta annars árs verður gerður samanburður á getu þorskatrypsín blöndu og mismunandi afbrigða þess til að rjúfa valin svipmótuð prótein sem tengjast sáravessa og græðingu sára.

Niðurstöður verkefnisins munu leiða til útskriftar MS nema árið 2012 og birtingar greinar í viðurkenndu erlendu vísindariti.

Heimildir

[1] Wyatt G. Payne et al. Eplasty (2008) vol. 8. Enzymatic Debriding Agents are Safe in Wounds with High Bacterial Bioburden and Stimulate Healing.
[2] Mangioli, M. (2004). Evaluation of an enzyme extracted from fish for topical use in the treatment of pressure sores. Úr doktorsritgerð við Háskólann í Möltu.

Poster 23

Comparison between cod trypsin isoforms to degrade native proteins

Guðrún Birna Jakobsdóttir[1,2], Ágústa Guðmundsdóttir[2,3], Bjarki Stefánsson[1] og Hilmar Hilmarsson[1]

[1]Department of Biochemistry, Science Institute, University of Iceland Dunhagi 3-5, 107Rvk.
[2]Faculty of Physical Sciences, School of Engineering and Natural Sciences, University of Iceland
[3]Faculty of Food Science and Nutrition, School of Helath Sciences, University of Iceland

The goal of this MS project is twofold: Firstly, to compare the ability of cod- and bovine trypsins to degrade native proteins. Secondly, to compare the ability of isolated trypsin isoforms to degrade native proteins, especially those connected to wound exudates.

Trypsins are serin proteases found in the digestive system of many vertabrates where they hydrolyse polypeptide chains on the C-end side of the amino acids lysine and arginine.

It is known that proteases speed up the process of wound healing by breaking down proteins in wound exudates [1]. Clinical trials on the use of cod trypsins in water-based gel solutions for wound healing have demonstrated positive effects [2].

During the early part of the projects first year, future work was prepared and methodology was developed. The latter part of the first year was focused on comparison between the ability of cod- and bovine trypsins to degrade different native proteins.

The studies were carried out at 4°C, 25°C and 37°C at different time intervals and degradation patterns were analyzed with HPLC.

These were also analyzed with gel electrophoresis.

The results clearly show that cod trypsin was more effective in cleaving native proteins than bovine trypsin. During the early part of the second year, different isoforms of cod trypsins were separated on a MonoQ column.

A trypsin mixture was previously isolated from 15 L of cod pyloric caeca extract on a *p*-aminobenzamidine column.

Comparison between the ability of trypsins and trypsin isoforms to cleave native proteins connected to exudate and wound healing will be undertaken during the latter part of the second year.

The results of this research project will lead to graduation of a MS student in 2012 and a publication in a peer reviewed scientific journal.

References

[1] Wyatt G. Payne et al. Eplasty (2008) vol. 8. Enzymatic Debriding Agents are Safe in Wounds with High Bacterial Bioburden and Stimulate Healing.
[2] Mangioli, M. (2004). Evaluation of an enzyme extracted from fish for topical use in the treatment of pressure sores. A dissertation submitted in fulfilment of the degree of B. Pharm (Hons) at the University of Malta.

Veggspjald 24

Griptæknivinnsla og eiginleikar kítínasa úr *T. emersonii*

Hörður Filippusson, Róbert Anton Hafþórsson og Guðný Björg Sigurðardóttir

Háskóli Íslands, Raunvísindastofnun, Lífefnafræðistofa, Dunhaga 3, 107 Reykjavík

Kítín hefur verið hluti lífheimsins í um milljarð ára og finnst mjög víða í náttúrunni. Kítín og kítósan, sem er afasetýlerað kíín, hafa verið hagnýtt með ýmsu móti. Kítínasa er að finna í ýsum tegundum lífvera sem þurfa að geta melt eða ummyndað kítín. Kítínasalík prótein (*chitinase like proteinss, CLP's*) eru jafnvel enn útbreiddari og finnast líka í vefjum manna. Talið er að þau hafi lífeðlisleg hlutverk í myndun og endurnýjun vefja. Af þessum sökum hafa kítófásykrur verið í þróun og prófun sem áhrifsefni eða stýriefni þessara próteina sem gætu hugsanlega nýst semlyfjaefni. Kítófásykrur úr hlutafasetýleruðu kítíni eða kítósani eru framleidd með kítínasahvöttu vatnsrofi. Markmið verkefisins sem hér er kynnt er að þróa griptækniaðferð til hreinvinnslu kítínasa og CLP svo unnt verði að kanna eiginleika þeirra með tilliti til vatnsrofssérhæfni og einnig bindigetu og bindifikn gagnvart kítófásykrum.

Vaxtaræti sveppsins *T. emersonii* var notað sem uppspretta kítínasa. Kítínasavirkni mæld með hvarfefninu h p-nitrophenyl-tri-N-acetyl--chitotrioside sýndi breitt kjörsýrustig milli 4 og 8 og góðan pH-stöðugleika og varmastöðugleika. TchOS, kítófásykra með DP (degree of polymerization) 6-15 og meðalmólmassa um 4000, er framleitt af Genis ehf ltd með rækilegri meltingu hlutafasetýleraðs kítíns. TchOS var kyrrsett á epichlorohydrin-virkjaðan Sepharose CL-6B, bæði beint og einnig með millitengingu um *cyanuric chloride*. Síðara efnið val valið til frekari rannsóknar. Þannig myndað gripefni, TCES, var notað til að veiða ensím úr vasxtaræti *T. emersonii* og reyndist binda 6 ml af próteini á hvern ml gripefnis. Prótein skolað af gripefninu reyndist með SDS-rafdrætti innihalda þrjú prótein með mólmassa frá 35 KDa til 60KDa. Próteinin voru aðgreind frekar með hlaupsíun til greiningar með tilliti til ensímvirkni og kítinbindieiginleika með *isothermal titration calorimetry*.

Poster 24

Affinity Chromatography and Characterization of Chitinases from *T. emersonii*

Hörður Filippusson, Róbert Anton Hafþórsson and Guðný Björg Sigurðardóttir

University of Iceland, Science Institute, Biochemistry Department, Reykjavík, Iceland

Chitin has been part of the living world for some one billion years and is widely present in Nature. Chitin and chitosan, a deacetylated chitin product, have found various practical uses. Chitinases are found in various species which need to digest or modify chitin but chitinase like proteins (CLPs) are even more widespread, including in human tissues, and are thought to play physiological roles in tissue formation and regeneration. Therefore, chitooligaosaccharides are being developed and tested as effectors of these proteins with possible therapeutic roles. Production of oligosaccharides from partially deacetylated chitin and chitosan is carried out by chitinase hydrolysis. The purpose of the present project is to develop affinity purification methods for chitinases and CLPs to enable their characterization with respect to hydrolytic specificity and affinity for oligosaccharide ligands.

A growth medium of the fungus *T. emersonii* was used as a source of chitinase. The chitinase activity measured with p-nitrophenyl-tri-N-acetyl--chitotrioside as substrate showed a broad pH-optimum beetween 4 and 8 and good pH and temperature stability.

TchOS, a chitooligomer of DP (degree of polymerization) of 6-15 and average MW of some 4000, is produced by Genis ltd of Iceland by exhaustive enzymatic hydrolysis of partially deacetylated chitin. TchOS was immobilized on epichlorohydrin-activated Sepharose CL-6B, both directly and via cyanuric cloride. The latter was chosen for further study. This affinity medium, TCES, was applied to the T. emersonii growth medium and was found to bind 6 mg of protein per ml of gel. The eluted protein was found by SDS-electrophoresis to contain three different proteins of MW from 35 KDa to 60KDa. These proteins were further resolved by gel filtration for analysis for chitinase activity and for chitin-binding properties by isothermal titration calorimetry.

Veggspjald 25

Stöðgun próteina með kítófásykrum

Hörður Filippusson og Stefán Bragi Gunnarsson

Háskóli Íslands, Raunvísindastofnun, Lífefnafræðistofa, Dunhaga 3, 107 Reykjavík

Öll prótein, þar með talin ensím, eru meira eða minna óstöðug, einkum í upplausn. Smám saman eiga sér stað breytingar á þrívíddarbyggingu sameindanna sem síðan leiða til ógagnhverfrar eðlissviptingar með missi líffræðilegrar virkni. Stöðugleiki próteina og aðferðir til að auka hann eru því mikilvægt viðfangsefni sem menn hafa tekist á við með mismunandi hætti, t.d. próteinverkfræði, kyrrsetningu, efnafræðilegum breytingum svo sem áfestingu annarra efna (*chemical modification*) og notkun verndarefna (*cosolutes*). Meðal þess sem áhrif getur haft á stöðugleika er próteinasavirkni (m.a. sjálfmeltu (*autodigestion*) ef um próteinasa er að ræða), virknitap af völdum upphitunar (t.d. þegar próteinið er hitað til að drepa veirur) eða við geymslu við stofuhita, próteinniðurbrot in vivo og mótefnavakning (*antigenicity*) eftir inndælingu ofl.

Einkum er þetta mikilvægt á tveim sviðum: a) við notkun ensíma í hagnýtum tilgangi og b) við framleiðslu próteinlyfja.

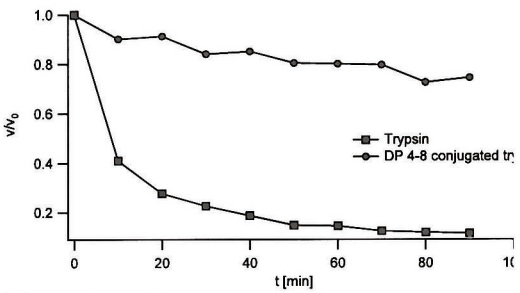
Ensím eru notuð í miklum og vaxandi mæli sem lífhvatar til efnagreininga og í iðnaðarferlum til hvötunar við framleiðslu ýmissa efna, sem notuð eru við lyfjagerð, í matvælaiðnaði og á fleiri sviðum. Bættur stöðugleiki ensíma er því mikilvægt viðfangsefni.

Með tilkomu erfðatækni hefur reynst unnt að framleiða hin ólíkustu prótein til lyfjanota í miklu magni svo hagkvæmt er til sölu á lyfjamarkaði og eru próteinlyf (stundum nefnd líftæknilyf) einn helsti vaxtarbroddur í lyfjagerð nú um stundir. Meðal viðvarandi vandamála er skortur á stöðugleika próteinanna, til dæmis í lyfjaformum eða eftir inntöku eða gjöf.

Fyrirtækið Genis ehf hefur unnið að þróun fásykra (*chito-oligosaccharides*, kítófaásykra) úr kítósani, fjölsykru sem unnin er með umbreytingu kítíns úr rækjuskel. Afurðir fyrirtækisins eru ætlaðar til lyfjanota. Við höfum í þessu verkefni kannað möguleika á því að nota fásykrur frá Genis til stöðgunar próteina.

Gerðar hafa verið tvenns konar tilraunir. Annars vegar hefur verið rannsakað virknitap ensímanna trypsins og peroxídasa við mismunandi hitastig. Hins vegar hefur verið beitt varmamælitækni, DSC (differential scanning calorimetry) til að finna við hvaða hitastig próteinin eðlissviptast. Áhrif kítófásykra (chitooligosaccharides) í upplausn á stöðugleika próteinanna hafa verið könnuð og einnig áhrif þess að tengja kítófásykrur með samgildum tengjum við ensímin.

Niðurstöður sýna eindregin stöðgunaráhrif í báðum tilvikum, þ.e. með kítófásykrur sem verndarefni í upplausn og einnig eftir umbreytingu ensímanna með tengingu við kítófásykrur. **Mynd 1** sýnir áhrif þess að tengja kítófásykru með DP (*degree of polymerisation*) 4 - 8 á hitastöðugleika trypsins:



Mynd 1. ! #$&"'"()*+,-./,$01',/'*(2 * 3,$&4*(-*+A*567&*&"$&4*96*2 :/;$#-*

Auk virknimælinga sem fall af hitastigi hafa einnig verið gerðar mælingar með DSC (*differential scanning calorimetry*) sem sýna svokallað bræðslumark ensímsins, þ.e. það hitastig er eðlissvipting á sér stað.

Með rannsóknum á ensímunum trypsini og peroxídasa hefur verið sýnt fram á grundvöll verkefnisins. Í framhaldinu þarf að gera mælingar á öðrum próteinum, bæði sams konar og einnig annars konar mælingar. Velja þarf nokkur prótein ólíkrar gerðar og gera á þeim eftirtaldar athuganir, frjálsum, í lausn með kítófásykrum og eftir tengingu við kítófásykrur: Hitastöðugleikamælingar (ensím), *differential scanning calorimetry*, mótefnamyndun (*antigenicity*) og stöðug-leika gagnvart próteinkljúfandi ensímum.

Poster 25

Protein stabilization with chitooligosaccharides

Hörður Filippusson and Stefán Bragi Gunnarsson

University of Iceland, Science Institute, Biochemistry Department, Reykjavík, Iceland

All proteins, enzymes included, are more or less unstable, especially when in solution. Gradual changes in the three-dimensional structure of the molecules lead to irreversible denaturation and loss of biological activity. Protein stability and methods for increasing it are therefore important problems which have been tackled in various ways, including protein engineering, immobilization, chemical modification and the use of cosolutes. Among the processes which can affect stability are protease action (including autodigestion of proteases), thermal denaturation (e.g. when the protein is heated to kill viruses) or storage at room temperature, protein degradation *in vivo* and antigenicity after etc.

This is especially important in two areas: a) in the use of enzymes aas practical biocatalysts and b) in the production and use of protein pharmaceuticals.

Enzymes are used increasingly as biocatalysts in chemical analyses and in industrial processes for the production of a multitude of chemicals to be used in the synthesis of pharmaceuticals, in the food industry and in other areas. Improving the stability of enzymes is therefore an important problem.

With the advent of recombinant technology it has become practical to produce a variety of proteins for use as pharmaceuticals in a cost-effective way for the drug market. Protein drugs or biopharmaceuticals are one of the most important greowth areas among pharmaceuticals. A persistent problem is lack of stability during storage or after injection.

Genis ehf has been developing chitooligosaccharides from chitosan, a polysaccharide produced by conversion of chitin from shrimp. The comany´s products are intended for pharmaceutical use. In the presen project we have investigated the possibility of using chitooligosaccharides for the stabilization of proteins.

Two kinds of experiments have been carried out. On the one hand we have measured the loss of activity of the enzymes trypsin and peroxidase at different temperatures. On the other hand we have used DSC (*differential scanning calorimetry*) to detact the temperature where the enzymes denature. The effect of chitooligosaccharides in solution on the stability of the proteins have been investigated as well as the effect of modifying the enzymes by covalent chemical conjugation with the oligosaccharides.

The results show clear stabilization effects, both with chitooligosaccharides as cosolutes and after their chemical coupling to the enzymes. **Fig. 1** shows the effect of chemical coupling of a chitooligosaccharide of DP (degree of polymerization) of 4-8 on the thermostability of trypsin.

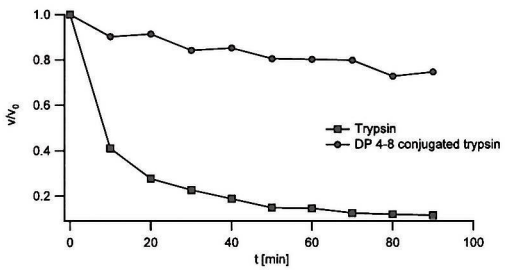


Fig 1. !"#$%#& ()*#$+(',)$)(-$. /$(%-0+)1$2 "#1 "#' (#3$(.$1 "#$%&' (%)*%&'%, "%- ./)+0123

In addition to activity measurements as a function of temperature we have made DSC (*differential scanning calorimetry*) measurements which show a so-called melting point of the enzymes, i.e. the temperature at which denaturation occurs.

Experiments with trypsin and peroxidase have proven the concept. Further work will include experiments on other proteins, both of the same kind and also other measurements. Several different proteins will be chosen for heat stability measurements, DSC, antigenicity testing and stability towards proteases. These will be carried out on fre and chemically modifies proteins as well as in solution with cosolutes.

Veggspjald 26

Efnasmíðar á náttúrulegum handhverfuhreinum ein- og fjölómettuðum metoxyl-setnum alkylglýserólum

Carlos D. Magnússon, Einar Lúthersson og Guðmundur G. Haraldsson

Raunvísindastofnun Háskóla Íslands, Dunhaga 3, 107 Reykjavík, Ísland

Metoxyl-setin alkylglýseról af gerð (2′*R*)-1-*O*-(2′-metoxyalkyl)-*sn*-glýseróla tilheyra flokki 1-*O*-alkyl-*sn*-glýseróla, svonefnd glýseryl eterar, og hafa þau metoxyl hóp í stöðu 2 á *O*-alkyl keðjunni.

Hliðstætt öðrum 1-*O*-alkyl-*sn*-glýserólum þá hefur verið sýnt fram á að þessi efni hafa margvíslega líffræðilega virkni. Til þessarar virkni teljast bakteríudrepandi, sveppadrepandi og krabbameinshemjandi áhrif [1].

Metoxyl-setin alkylglýseról finnast víða í náttúrunni. Þau hafa aðallega verið einangruð úr lifrarolíu sumra brjóskfiskstegunda þar sem þau finnast í verulegu magni og eru um 2-4% glýseryl etera [1].

Algengustu 1-*O*-(2′-metoxyalkyl)-*sn*-glýserólin bera keðjurnar hexadek-4-enyl (C16:1), hexadekyl (C16:0) og octadek-4-enyl (C18:1). Fjölómettuð dókosahexaensýru (DHA) lík metoxyl-setin alkylglýseról afleiða er einnig algeng í lifrarolíu sumra brjóskfiska þar sem hún getur orðið allt að 18% metoxyl-setinna glýseryl etera. Þessi einstaka fjölómettaða afleiða hefur einnig fundist í fósfólípíðum rauðra blóðkorna í mönnum þar sem þau hafa mælst um 8% metoxyl-setinna glýseryl etera [1].

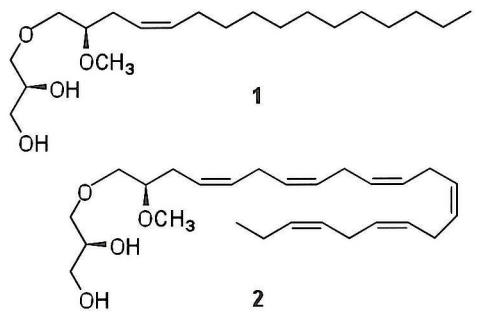
Megin markmið framlagsins er tvíþætt. Í fyrsta lagi að gera grein fyrir fyrstu efnasmíði á handhverfuhreinu einómettuðu (*Z*)-(2′*R*)-1-*O*-(2′-metoxyhexadec-4′-enyl)-*sn*-glýseróli **1** sem er algengasta metoxyl-setna alkylglýserólið í náttúrunni [2]. Í öðru lagi að gera grein fyrir þýðingarmiklum skrefum í heildarefnasmíði á handhverfuhreinu fjölómettuðu (2′*R*)-1-*O*-(2′-metoxydókosahexa-4′,7′,10′,13′,16′,19′-enyl)-*sn*-glýseróli **2**.

Metoxyl-setna alkylglýserólið **1** var smíðað á skilvirkan hátt í fimm skrefa efnasmíði í 27% heildar heimtum [2]. Lykilskrefið fól í sér myndun etertengis á milli (*Z*)-(*R*)-1-klórohexadek-4-en-2-óls og handhverfuhreins (*R*)-2,3-*O*-ísóprópyliden-*sn*-glýseróls í viðurvist malaðs kalíum hydroxíðs, ásamt tetra-*n*-bútylammoníum brómíði án notkunar lífræns leysis við herbergishita [2].

Heildarefnasmíði fjölómettaðs metoxyl-setins alkylglýseróls **2** er skipt í tvo hluta. Fyrri hlutinn felur í sér efnasmíði á fjölalkeni, Z-skipuðu (2*R*)-1-klórodókosa-4-7-10-13-16-19-hexaen-2-óli, sem fæst með rúmvendaðri vetnun á samsvarandi fjölalkyni (2*R*)-1-klórodókosa-4-7-10-13-16-19-hexayn-2-ól með Lindlar-hvata.

Efnasmíðinni á fjölalkyninu er verið að ljúka með góðum árangri og heimturnar fyrir milliefnin eru á bilinu 65-84%. Þessi tíu skrefa efnasmíði byggir á röð málmhvataðra kúplunarhvarfa á milli endastæðra alkyna og própargyl brómíða í viðurvist Cu(I)I, NaI og K_2CO_3 eða Cs_2CO_3 sem basar.

Seinni hluti efnasmíðinnar á **2** verður byggður á aðferðinni sem þróuð var við efnasmíðina á **1** sem sagt þéttingu á milli áðurnefnds fjölalkens og handhverfuhreins (*R*)-2,3-*O*-ísóprópyliden-*sn*-glýseróls í viðurvist malaðs kalíum hydroxíðs, ásamt tetra-*n*-bútylammoníum brómíði.



Byggingar lokamyndefnis **1**, milliefna þess og milliefna í heildarefnasmíðinni á **2**, hafa verið sannreyndar með hefðbundnum aðferðum lífrænar efnafræði, þar með talið kjarnarófsmælingum (^{1}H NMR og ^{13}C NMR), IR litrófmælingum, ljósvirknimælingum og massagreiningum (HRMS).

References

[1] C D Magnusson and G G Haraldsson. Chem. Phys. Lipids (2011) 164, 313-40.
[2] C D Magnusson and G G Haraldsson. Tetrahedron Asymmetry (2010) 21, 2841-47.

Poster 26

Synthesis of naturally occurring enantiomerically pure mono- and polyunsaturated 2′-methoxylated alkylglycerols

Carlos D. Magnússon, Einar Lúthersson and Guðmundur G. Haraldsson

Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland

The 2′-methoxylated alkylglycerols of the (2′*R*)-1-*O*-(2′-methoxyalkyl)-*sn*-glycerol type are a particular category of 1-*O*-alkyl-*sn*-glycerols, also called glyceryl ethers, characterized by bearing a methoxyl group at the 2-position of their *O*-alkyl moiety.

Like their unsubstituted analogues, they have been reported to exhibit multiple biological activities. For instance, they have been shown to possess antibacterial, antifungal, anticarcinogenic and immune stimulant properties [1].

The 2′-methoxylated alkylglycerols are widely found in Nature. They have principally been isolated from the liver oil of some cartilaginous fish species where they are found in appreciable amounts accounting for 2-4% of the glyceryl ethers content [1].

The most prevalent 1-*O*-(2′-methoxyalkyl)-*sn*-glycerols comprise hexadec-4-enyl (C16:1), hexadecyl (C16:0) and octadec-4-enyl (C18:1) chains. A polyunsaturated docosahexaenoic acid (DHA) like 2′-methoxylated alkylglycerol has also been found to constitute up to 18% of the methoxylated glyceryl ethers in the liver oil of some cartilaginous fish. This peculiar methoxylated alkylglycerol has also been found in the phospholipids of human red blood cells where they account for about 8% of the methoxylated glyceryl ethers [1].

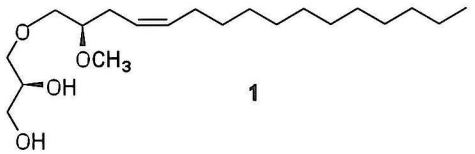
The main objective of the current presentation is, firstly, to describe the first synthesis of enantiomerically pure monounsaturated (*Z*)-(2′*R*)-1-*O*-(2′-methoxyhexadec-4′-enyl)-*sn*-glycerol **1**, the most prevalent 2′-methoxylated alkylglycerol found in Nature, and, secondly, to describe an important milestone in the synthesis of enantiopure polyunsaturated all *cis* (2′*R*)-1-*O*-(2′-methoxydocosahexa-4′,7′,10′,13′,16′,19′-enyl)-*sn*-glycerol **2**.

An efficient five-step synthetic approach was developed to accomplish the synthesis of **1** taking place in 27% overall yield [2]. The strategy was based on an ether bond formation between the highly functionalized key fragment, (*Z*)-(*R*)-1-chlorohexadec-4-en-2-ol, and enantiopure (*R*)-2,3-*O*-isopropylidene-*sn*-glycerol employing grounded potassium hydroxide and tetra-*n*-butylammonium bromide under solvent free conditions [2].

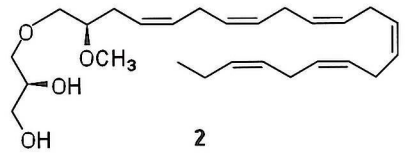
The planned synthetic route to compound **2** is divided into two parts. The first part involves the synthesis of the methylene interrupted polyene all *cis* (2*R*)-1-chlorodocosa-4-7-10-13-16-19-hexaen-2-ol which, in turn, could be prepared by stereoselective partial hydrogenation of the corresponding polyyne (2*R*)-1-chlorodocosa-4-7-10-13-16-19 hexayn-2-ol using Lindlar′s catalyst.

The synthesis of the highly functionalized polyyne has been successfully concluded after a ten-step process with yields ranging from 65 to 84% for the intermediates involved. This synthesis is based on consecutive cross-coupling reactions between terminal alkynes and propargylic bromides in the presence of Cu(I)I, NaI and K_2CO_3 or Cs_2CO_3 as bases.

The second part of the proposed route to **2** is based on the previously developed approach for the monounsaturated analogue **1** and includes the condensation of the methylene interrupted polyene with (*R*)-2,3-*O*-isopropylidene-*sn*-glycerol in the presence of grounded potassium hydroxide and tetra-*n*-butylammonium bromide.



1



2

The target compound **1**, all its intermediates and the intermediates toward the total synthesis of **2** have been fully characterized by traditional organic synthesis methods including ^{1}H and ^{13}C NMR, IR spectroscopy, optical activity measurements and HRMS.

References

[1] C D Magnusson and G G Haraldsson. Chem. Phys. Lipids (2011) 164, 313-40.

[2] C D Magnusson and G G Haraldsson. Tetrahedron Asymmetry (2010) 21, 2841-47.

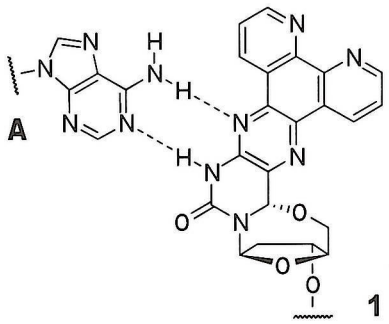
Veggspjald 27

5'-6 Læstar Kirnisleifar: Fjölhæf Nálgun til Efnasmíða á Nemum fyrir Kjarnsýrurannsóknir

Kristmann Gíslason* og Snorri Þór Sigurðsson

Raunvísindastofnun, Háskóli Íslands, Dunhagi 3, 107 Reykjavík, Ísland

Á sviði lífeðlisfræðilegra rannsókna á byggingu kjarnsýra er stöðugt verið að leita að nýjum breyttum kirnisleifum sem nýst geta sem áhugaverðir nemar [1]. Einnig er áhugi fyrir notkun breyttra kirnisleifa sem virkra byggingareininga í DNA nanó-byggingum [2]. Með því að nýta okkur efnahvarf þar sem 5-amínó-2'-deoxycytidín er þétt með díketón [3], höfum við smíðað 5'-6-læstu stífu kirnisleifina 1. Þessi kirnisleif inniheldur fenanþrólín hluta sem nýst getur til innleiðingar málmkomplexa á 5'-enda kjarnsýra [4]. Þegar þessi kirnileif er innleidd í fákirni, myndar hún stöðugt basapar líkt tymidíni (Mynd 1) og veldur aðeins minniháttar breytingum á náttúrulegri byggingu B-DNA helix. Stífleiki kirnisleifarinnar tryggir hámarks næmni fyrir breytingum í byggingu og hreyfingu kjarnsýrunnar. Við höfum einnig nýtt þessa nálgun til að smíða safn fljúrljómandi kirnisleifa og kirnisleif sem getur bundið jónir lanþaníðmálma.



Mynd 1. Kirnisleifin 1 basapöruð við adenósín (A).

Tilvitnanir

[1] F. Wachowius, and C. Höbartner, ChemBioChem 11, 469 (2010)
[3] Z. J. Lesnikowski, Current Organic Chemistry 11, 355 (2007)
[3] G. Ping, et al., Nucleosides & Nucleotides 15, 1701 (1996)
[4] K. Gislason, and S. T. Sigurdsson, Eur. J. Org. Chem. 2010, 4713 (2010)

Poster 27

5'-6 Locked Nucleosides: A Versatile Approach to Nucleic Acid Probes

Kristmann Gíslason* and Snorri Þór Sigurðsson

Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavik, Iceland

The search for new and interesting modified nucleosides as probes for various biophysical techniques, used to study nucleic acid structures is ongoing [1]. Modified nucleosides are also of interest as functional units in nucleic acid nano-structures [2]. Utilizing a reaction where 5-amino-2'-deoxycytidine is condensed with diketones [3], we have synthesized 5'-6 locked rigid nucleoside 1 containing a phenanthroline moiety for incorporation of metal complexes onto the 5'-end of nucleic acids [4]. This nucleoside, when incorporated into oligonucleotides, forms stable base-pairs similar to thymidine (Figure 1), with only minimal distortion to natural B-DNA helix structure. The rigid structure of the nucleoside ensures optimal sensitivity to changes in the structure and dynamics of the nucleic acids. We have also used this strategy to prepare a series of fluorescent nucleosides and a nucleoside that can be used as a chelator for lanthanide metal ions.

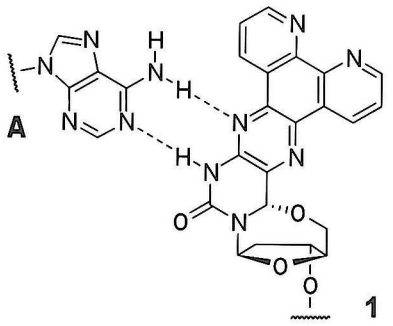


Figure 1. Nucleoside 1 base-paired to adenosine (A).

References

[1] F. Wachowius, and C. Höbartner, ChemBioChem 11, 469 (2010)

[3] Z. J. Lesnikowski, Current Organic Chemistry 11, 355 (2007)

[3] G. Ping, et al., Nucleosides & Nucleotides 15, 1701 (1996)

[4] K. Gislason, and S. T. Sigurdsson, Eur. J. Org. Chem. 2010, 4713 (2010)

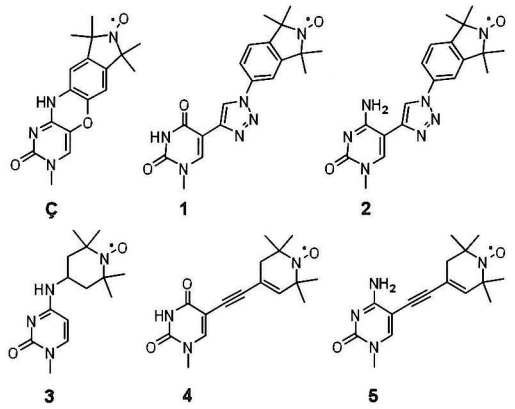
Veggspjald 28

Nitroxíð spunamerki sem binds við ákveðinn stað á kjarnsýrum án samgildra tengja

Gunnar B. Sandholt, Sandip A. Shelke and Snorri Th. Sigurdsson

*Raunvísindasofnun, Háskóli Íslands, Dunhagi 3, 107 Reykjavík, Ísland

Rafeindaspunatækni hefur verið notuð til að kynnast byggingu og hreyfanleika líffrænna fjölliða [1-3]. Rannsóknir á líffrænum fjölliðum, með rafeindasegulgreini, krefjast þess að sameindirnar innihaldi óparaða rafeind (spunamerki). Merkin eru venjulega innleidd með samgildum tengjum á fyrirfram ákveðnum stað [4]. Enn sem komið er þarfnast sú aðferð mikllar efnasmíðar frá reyndu fólki. Við höfum þróað aðferð sem tengir spunamerki við kjarnsýru án samgildra tengja. Sú aðferð notast við spunamerkið ç og kjarnsýru án kirnibasa þar sem merkið bindst með vetnistengjum og van der waals kröftum [5].



Mynd 1. ç ásamt spunamerkjum sem einfalt er að smíða og innleiða í DNA án kirnibasa til samanburðar.

Aðferðin leysir vandamál sem fylgja samgildum spunamerkingum. Við leit okkar að spuna-merkjum sem bindst betur við kjarnsýrur án kirnisbasa en ç, auk að þess hafa styttri efnasmíð, höfum við smíðað nokkur mismunandi spunamerki sem hafa það sameiginlegt að vera pýrimidín kirnibasa-afleiður. Spunamerkin voru smíðuð með tveimur megin aðferðum. Annars vegar azíð-alkýn Huisgen-Meldal-Sharpless (3+2) hringmyndunarhvarfi (smelli efnafræði) (**1**, **2**) og hins vegar palladíumhvötuðu Sonogashira hvarfi (**4**,**5**). Spunamerkin voru greind með rafeindasegulgreini, þar sem rófið sýndi þrjár skarpar línur. Mat á bindingu spunamerkjana við kjarnsýrur án kirnibasa er í vinnslu.

Heimildir

[1] Biswas, R., Kühne, H., Brudvig, G. and Gopalan, V., Use of EPR spectroscopy to study macromolecular structure and function. Sci. Prog., 2001. 84: p. 45-67.

[2] Klare, J.P. and Steinhoff, H.J., Spin labeling EPR. Photosyn. Res., 2009. 102(377-390).

[3] Qin, P.Z. and Dieckmann, T., Application of NMR and EPR methods to the study of RNA. Current Opinion in Structural Biology, 2004. 14: p. 350-359.

[4] Shelke, A.S. and Sigurdsson, S.Th., Site-Directed Nitroxide Spin-Labeling of Biopolymers, in Unpublished book chapter. 2011.

[5] Shelke, S.A. and Sigurdsson, S.Th., Noncovalent and Site-Directed Spin Labeling of Nucleic Acids. Angew. Chem. Int. Ed., 2010. 49: p. 7984-7986.

Poster 28

Nitroxide spin-labels for noncovalent and site directed spin-labeling of nucleic acids

Gunnar B. Sandholt, Sandip A. Shelke and Snorri Th. Sigurdsson

*Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavík, Iceland

Electron paramagnetic resonance (EPR) spectroscopy has been used to study the structure and dynamics of biopolymers [1-3]. The study of biopolymers with EPR spectroscopy requires an unpaired electron (spin labels). The labels are usually incorporated by covalent attachment at a specific site, generally termed site-directed spin labeling (SDSL) [4]. So far such SDSL requires a large synthetic effort and skilled manpower. We have developed a noncovalent site-directed spin labeling (NC-SDSL) approach by utilizing spin-label ç and DNA containing an abasic site where it binds by base-paring and stacking interactions [5].

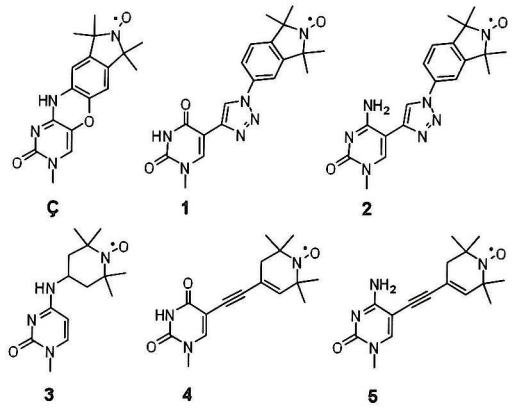


Figure 1. ç along with simple to make spin-labels for incorporation in to abasic site dsDNA for comparison.

This approach helps to get around the problem associated with covalent labeling. In an attempt to find spin labels that have better binding affinity and shorter synthesis than ç, we designed several spin-label ligands by modifying the pyrimidine nucleobases. The spin labels were prepared by using two main strategies using either azide-alkyne Huisgen-Meldal-Sharpless (3+2) cycloaddition reaction (click chemistry) to prepare **1** and **2** or palladium catalyzed Sonogashira coupling to make **4** and **5**. The spin labels were analyzed by EPR spectroscopy, which shows three sharp lines in their EPR spectrum. Evaluation of their binding to an abasic site in duplex DNA is in progress.

References

[1] Biswas, R., Kühne, H., Brudvig, G. and Gopalan, V., Use of EPR spectroscopy to study macromolecular structure and function. Sci. Prog., 2001. 84: p. 45-67.

[2] Klare, J.P. and Steinhoff, H.J., Spin labeling EPR. Photosyn. Res., 2009. 102(377-390).

[3] Qin, P.Z. and Dieckmann, T., Application of NMR and EPR methods to the study of RNA. Current Opinion in Structural Biology, 2004. 14: p. 350-359.

[4] Shelke, A.S. and Sigurdsson, S.Th., Site-Directed Nitroxide Spin-Labeling of Biopolymers, in Unpublished book chapter. 2011.

[5] Shelke, S.A. and Sigurdsson, S.Th., Noncovalent and Site-Directed Spin Labeling of Nucleic Acids. Angew. Chem. Int. Ed., 2010. 49: p. 7984-7986.

Veggspjald 29

Efnasmíðar handhverfuhreinna diasýl glyseryl etera sem innihalda fjölómettaðar fitusýrur

Edda Katrín Rögnvaldsdóttir, Carlos D. Magnússon, Sara Björk Sigurðardóttir og Guðmundur G. Haraldsson

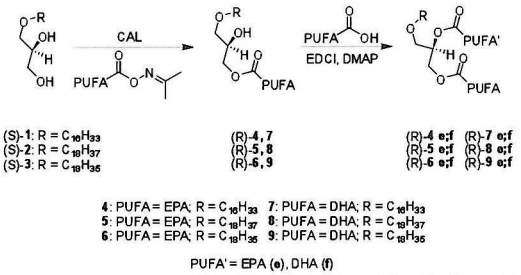
Raunvísindastofnun Haskólans, Dunhaga 3, 107 Reykjavík, Ísland.

Náttúruleg 1-*O*-alkýl-*sn*-glýseról finnast víða í náttúrunni sem svonefnd eterlípíð. Eterlípíðin hafa sýnt fjölbreytta líffræðilega virkni, þar með talið bakteríu- og sveppadrepandi, krabbameinshemjandi og ónæmisstyrkjandi áhrif. Þau eru almennt talin hafa mikla lækningamöguleika.

Eikósapentaensýra (EPA) og dókósahexaensýra (DHA) eru ómega 3 (n-3) fitusýrur sem eru einkennandi fyrir fitu úr sjávarlífverum. Þessar lífvirku fitusýrur hafa vakið mikla athygli vegna jákvæðra heilsufarsáhrifa á menn, einkum í tengslum við hjarta- og æðasjúkdóma, sjálfsónæmissjúkdóma og bólgusjúkdóma, við sumum gerðum krabbameina sem og góð áhrif á geðheilsu manna [1].

Eterlípíð af 1-*O*-alkýl-2,3-diasýl-*sn*-glýseról-gerð, sem innihalda langar n-3 fjölómettaðar fitusýrur (PUFA), eru líffræðilega áhugaverð efni, því þau sameina heilsufræðileg áhrif 1-*O*-alkýl-*sn*-glýseróla og PUFA [2].

Mynda má tólf mismunandi gerðir 1-*O*-alkýl-2,3-diasýl-*sn*-glýseróla með handhverfuhreinum kímýl- (16:0), batýl- (18:0) og selakýl-alkóhólum (18:1) og EPA og/eða DHA í mið- og endastöðu. Annars vegar sex afleiður af ALL-gerð (alkyl-löng-löng), þar sem sama PUFA er í mið- og endastöðu, og hins vegar sex afleiður af ALL'-gerð, þar sem mismunandi PUFA eru notaðar.



Mynd 1. Efnasmíðar handhverfuhreinna diasýl glyseryl etera af ALL og ALL' gerð.

Kyrrsettur Candia antarctica lípasi (CAL) er notaður til að innleiða PUFA inn á endastöðu 1-O-alkýl-sn-glýseróls, í formi virkjaðra asetoxím estera. Síðan er sömu eða annarri PUFA komið fyrir í miðstöðu með kemískri estrun sem notast við EDCl sem kúplunarmiðil og DMAP sem basa.

Heimildir

[1] Magnusson, C.D., *Ether lipids: synthesis oj structured diacyl glyceryl ethers and methoxylated 1-O-alkyl-sn-glycerols,* PhD-thesis. University of Iceland, 2010

[2] Magnusson, C.D and Haraldsson, G.G., *Activation if n-3 polyunsaturated fatty acids as oxime esters: A novel approach for their incorporation into the glycerol moiety by lipase.* Manuscript submitted for publication.

Poster 29

Synthesis of enantiopure diacyl glyceryl ethers comprising polyunsaturated fatty acids

Edda Katrín Rögnvaldsdóttir, Carlos D. Magnússon, Sara Björk Sigurðardóttir and Guðmundur G. Haraldsson

Science Institute of the University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland

The naturally occurring 1-*O*-alkyl-*sn*-glycerols are widespread in nature and are generally known as ether lipids. They are usually minor lipid components, but are found in high amounts in the liver oil of some cartilaginous fish species. They exhibit multiple biological activities including, antibacterial and antifungal activities as well as anti-carcinogenic and immune stimulant activities. They are considered to have high therapeutic potential.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are n-3 polyunsaturated fatty acids that are characteristic of marine lipids. They are bioactive compounds that have gained increasing attention due to their beneficial health effects on humans regarding cardiovascular diseases, various inflammatory and autoimmune diseases and some types of cancer as well as importance to mental health [1].

Ether lipids of the 1-*O*-alkyl-2,3-diacyl-*sn*-glycerol type, containing long chain n-3 polyunsaturated fatty acids (PUFAs), are interesting compounds from the biological point of view, because they combine the beneficial effect of bioactive 1-*O*-alkyl-*sn*-glycerols and PUFAs [2].

Twelve different types of 1-*O*-alkyl-2,3-diacyl-*sn*-glycerols can be made by using enantiopure chimyl (16:0), batyl (18:0) and selachyl (18:1) alcohols and two different PUFAs, EPA and/or DHA, in the mid- and end-positions.

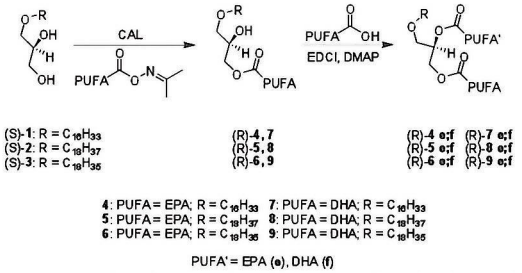


Figure 1. Synthesis of enantiopure diacyl glyceryl ethers of the ALL and ALL' type.

Therefore, a total of six adducts of the ALL type (alkyl-long-long), comprising the same PUFA in both positions, and another six adducts of the ALL' type, comprising different PUFAs in the mid- and end-positions can be made.

An immobilized Candida antarctica lipase (CAL) is used for the introduction of a PUFA into the end position of the glycerol backbone, using acetoxime ester of the corresponding PUFA. Then, the mid position is esterified, with the same or a different PUFA using EDCI as a coupling agent and DMAP as a base.

References

[1] Magnusson, C.D., *Ether lipids: synthesis of structured diacyl glyceryl ethers and methoxylated 1-O-alkyl-sn-glycerols,* PhD-thesis. University of Iceland, 2010

[2] Magnusson, C.D and Haraldsson, G.G., *Activation if n-3 polyunsaturated fatty acids as oxime esters: A novel approach for their incorporation into the glycerol moiety by lipase.* Manuscript submitted for publication

Veggspjald 30

HPLC–MS/MS analysis of 2-methoxylated alkylglycerols isolated from shark liver oil

Aðalheiður D. Albertsdóttir*, Sigurður V. Smárason† and Guðmundur G. Haraldsson*

* Science Institute, University of Iceland, Dunhaga 3, 107 Reykjavík, Iceland
† The European Academy of Bozen/Bolzano (EURAC), Drususallee 1, 39100 Bolzano/Bozen, Italy

The 1-*O*-alkyl-*sn*-glycerols, also known as glyceryl ethers, occur widely in Nature, but in particularly high amounts in the liver oil of various cartilaginous fish including shark species. Shark liver oil has been used in Scandinavia for centuries for its various remedial effects that have been attributed to the glyceryl ethers [1].

Minor parts (2 - 4 %) of the glyceryl ether fraction of such oils are substituted with a methoxyl group located at the 2-position of the alkyl moiety. Such methoxylated ether lipids, 1-*O*-(2'-methoxyalkyl)-*sn*-glycerols, are interesting compounds that have been claimed to offer multiple biological bioactivities including antifungal, antibacterial and antitumor properties. The general framework is shown in figure 1 [2].

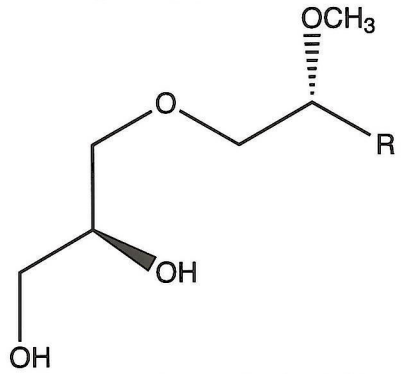


Figure 1. The basic framework of 1-*O*-(2'-methoxyalkyl)-*sn*-glycerols [2].

A HPLC–MS analytical method was developed to investigate a mixture of such 2-methoxy alkylglycerols (MAGs) isolated from the liver oil of deep sea sharks originating in the North Atlantic Ocean. The work was focused on the ammonium and lithium adducts of the MAGs.

Seven MAG adducts were found to account for the majority of the signals in the HPLC–MS analyses and accurate mass values were acquired for all of them. These compounds constitute two saturated (C16:0 and C18:0), three monounsaturated (C16:1 and two C18:1 isomers) and two polyunsaturated (C18:3 and C22:6) MAG derivatives.

Confirmation of the MAGs general framework was achieved by analyzing the ammonium adduct MSMS spectra while the lithium MSMS spectra provided information regarding the location of the double bonds in the mono- and polyunsaturated MAGs.

References

[1] Magnusson, C. D.; Haraldsson, G. G. *Chemistry and Physics of Lipids* **2011**, *164*, 315-340.
[2] Magnusson, C. D.; Haraldsson, G. G. *Tetrahedron: Assymmetry* **2010**, *21*, 2841-2847.

Poster 30

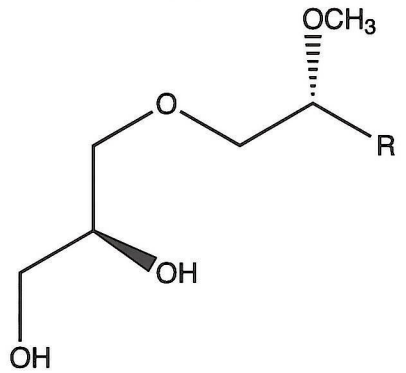
HPLC–MS/MS greining á 2-metoxylsetnum alkylglýserólum einangruðum úr hákarlalýsi

Aðalheiður D. Albertsdóttir*, Sigurður V. Smárason† og Guðmundur G. Haraldsson*

* Raunvísindastofnun, Háskóli Íslands, Dunhaga 3, 107 Reykjavík, Ísland
† The European Academy of Bozen/Bolzano (EURAC), Drususallee 1, 39100 Bolzano/Bozen, Italy

1-*O*-alkýl-*sn*-glyseról, einnig þekkt sem glyserýl eterar, koma víða fyrir í náttúrunni, en þessi efni finnast í sérstaklega miklu magni í lifrarolíu mismunandi brjóskfiska, þar á meðal í hákörlum. Hákarlalýsi hefur verið notað í Skandinavíu í margar aldir vegna ýmiskonar jákvæðra áhrifa sem hafa verið rakin til glyserýl etera [1].

Lítill hluti (2-4%) glyserýl etera í olíunni eru með metoxýl hóp staðsettan á kolefni 2 á alkýlkeðjunni. Þessi metoxýlsetnu eter lípíð, 1-*O*-(2'-metoxýalkýl)-*sn*-glýseról, eru athyglisverð efni sem hafa verið tengd við hina ýmsu lífvirkni meðal annars sem sveppaeyðandi, bakteríueyðandi og æxliseyðandi eiginleikar. Almenna bygging þeirra er sýnd á mynd 1 [2].



Mynd 1. Almenna bygging 1-*O*-(2'-metoxýalkyl)-*sn*-glyseróla [2].

HPLC-MS/MS greiningaraðferð var þróuð til þess að greina blöndu af þessum 2-metoxýleruðu alkýlglýserólum (MAGs) sem voru einangruð úr lýsi sem unnið var úr hákörlum sem veiddust í norður Atlantshafinu. Eingöngu voru rannsakaðar ammóníum- og liþíumjónir þessara efna.

Sjö MAG efni stóðu fyrir meginhluta merkjanna í HPLC–MS greiningunum og var nákvæmum massagildum náð fyrir þau öll. Þessi efni samanstóðu af tveimur mettuðum (C16:0 og C18:0), þremur einómettuðum (C16:1 og tveimur C18:1 ísómerum) og tveimur fjölómettuðum (C18:3 og C22:6) MAG afleiðum.

Staðfesting almennu MAG byggingarinnar fékkst með því að greina ammóníum MSMS rófin en liþíum rófin gáfu upplýsingar um staðsetningu tvítengja í ein- og fjölómettuðu MAG afleiðunum.

Tilvitnanir

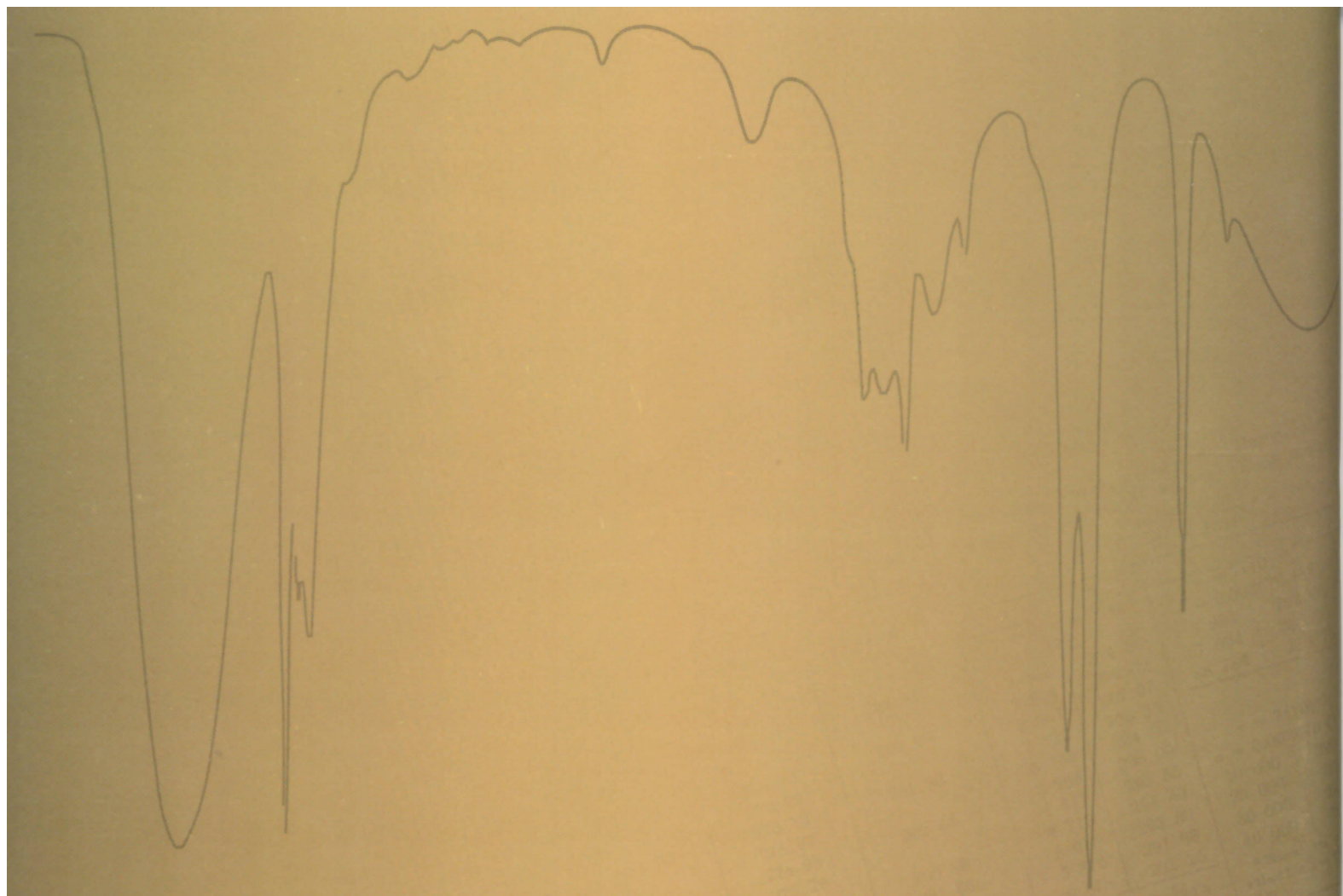
[1] Magnusson, C. D.; Haraldsson, G. G. *Chemistry and Physics of Lipids* **2011**, *164*, 315-340.
[2] Magnusson, C. D.; Haraldsson, G. G. *Tetrahedron: Assymmetry* **2010**, *21*, 2841-2847.

Hönnun og umbrot: Benedikt Ómarsson
Prentun: Pixel prentþjónusta ehf.
Upplag: 80 stk

Ráðstefna Efnís 2011

Efnafræðirannsóknir á Íslandi
tengsl grunnrannsókna og atvinnulífs

1 H 1.0079																	2 He 4.003
3 Li 6.941	4 Be 9.0122											5 B 10.811	6 C 12.011	7 N 14.007	8 O 15.999	9 F 18.998	10 Ne 20.179
11 Na 22.9898	12 Mg 24.3050											13 Al 26.982	14 Si 28.086	15 P 30.974	16 S 32.065	17 Cl 35.453	18 Ar 39.948
19 K 39.0983	20 Ca 40.078	21 Sc 44.9559	22 Ti 47.867	23 V 50.942	24 Cr 51.996	25 Mn 54.938	26 Fe 55.845	27 Co 58.9332	28 Ni 58.6934	29 Cu 63.546	30 Zn 65.38	31 Ga 69.723	32 Ge 72.640	33 As 74.922	34 Se 78.960	35 Br 79.904	36 Kr 83.798
37 Rb 85.4678	38 Sr 87.62	39 Y 88.9059	40 Zr 91.224	41 Nb 92.906	42 Mo 95.960	43 Tc (98)	44 Ru 101.070	45 Rh 102.906	46 Pd 106.420	47 Ag 107.868	48 Cd 112.411	49 In 114.818	50 Sn 118.710	51 Sb 121.760	52 Te 127.60	53 I 126.904	54 Xe 131.293
55 Cs 132.9054	56 Ba 137.327	57 La 138.9055	72 Hf 178.490	73 Ta 180.948	74 W 183.84	75 Re 186.207	76 Os 190.230	77 Ir 192.217	78 Pt 195.084	79 Au 196.967	80 Hg 200.59	81 Tl 204.383	82 Pb 207.20	83 Bi 208.980	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89 Ac (227)	104 Rf (265)	105 Db (268)	106 Sg (271)	107 Bh (272)	108 Hs (270)	109 Mt (276)	110 Ds (281)	111 Rg (280)							



Efnafræðifélag Íslands
The Icelandic Chemical Society