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MOLECULAR DYNAMICS STUDIES OF CALCIUM BINDING TO BETA PARVALBUMIN

Authors

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Abstract

Parvalbumin (PV) is a globular, calcium-binding protein expressed primarily in skeletal, but not cardiac muscle. While defects in PV function have been correlated with a variety of severe pathological conditions in non-muscle cell types, engineered sequences introduced to cardiac tissue have been shown to mitigate abnormal calcium signaling in animal models, which could potentially benefit heart patients. Our computational studies of the beta PV isoform seek to understand calcium binding at the protein's pseudo and canonical "EF" hand secondary structures. Specifically, we have employed molecular dynamics (MD) simulations to understand why calcium binds tightly in wild-type PV and even more tightly upon mutating an amino acid (Leucine-85-Phenylalanine) far from the calcium binding sites. Our MD simulations were analyzed to reveal changes in PV's three dimensional structure, as well as the density of protein oxygens that directly bind calcium. These data may provide a thermodynamic basis for how mutations affect calcium affinity and more importantly, could guide re-engineering of PV to mitigate defective calcium signaling in heart cells. Since the EF hand is common to a large class of proteins, we anticipate that our findings could shed light on related calcium-dependent proteins that modulate a wide range of physiological functions.

UNDERSTANDING THE STRUCTURAL CHANGES OF THE CALCIUM-BINDING PROTEINS S100A1 WITH MOLECULAR DYNAMICS SIMULATIONS

Authors

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Abstract

The S100A1 protein is ubiquitous in the human body and is particularly localized to heart and the brain tissue, within which it may influence the onset of debilitating cardiomyopathy or Alzheimer's disease. S100A1 is a homo-dimer that binds four calcium ions to drive a conformational change, whereby two helices separate to expose a target protein binding site. However, the physiochemical drivers of this conformational transition between the apo (no bound ions) to the holo (bound ions) states remain unclear. To understand the atomic basis of the conformational changes in S100A1, we performed nanosecond-scale molecular dynamics simulations (MD) of the apo-, half-saturated and fully-saturated holo states in explicit solvent. These MD studies reveal a variety of conformational trends including helical orientations, hydrogen bond contacts, and backbone fluctuations of the calcium binding regions. Based on our simulations, we speculate that occupation of the two calcium binding sites is necessary for stabilizing the holo conformation.

CHARACTERIZING PROTEIN CORONA FORMATION ON POLYSTYRENE NANOPARTICLES USING SINGLE-MOLECULE ANALYSIS

Authors

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Abstract

It is well known that nanoparticles in biological media form a protein coating, called a protein corona. The corona has been hypothesized to be one of the most important factors in determining a nanoparticle's fate and effect on cells. Here we have used fluorescence correlation spectroscopy (FCS), a non-invasive, single-molecule analysis technique, to characterize the adsorption of fluorescently labelled human transferrin and bovine serum albumin onto 50nm diameter polystyrene (PS) beads. The size of the corona was found to increase with protein concentration, with evidence of bilayer corona formation shown in both transferrin and albumin. The time span of corona formation was 120 minutes in transferrin and 180 minutes in albumin. Albumin coated PS beads showed significantly improved salt stability characteristics, an important result for medical potential. Results from this study will inform future studies of protein corona formation on nanoceria particles, specifically for drug delivery across the blood-brain barrier via transferrin-receptor mediated endocytosis

DEFINING STARCH BINDING BY GLUCAN PHOSPHATASES

Authors

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Abstract

Starch is a vital energy molecule in plants that has a wide variety of uses in industry, such as feedstock for biomaterial processing and biofuel production. Plants employ a three enzyme cyclic process utilizing kinases, amylases, and phosphatases to degrade starch in a diurnal manner. Starch is comprised of the branched glucan amylopectin and the more linear glucan amylose. Our lab has determined the first structures of these glucan phosphatases and we have defined their enzymatic action. Despite this progress, we lacked a means to quickly and efficiently quantify starch binding. The main objective of this study was to quantify the binding affinity of different enzymes that are involved in this cyclic process. We established a protocol to quickly, reproducibly, and quantitatively measure the binding of the enzymes to glucans utilizing Affinity Gel Electrophoresis (AGE) and Surface Plasmon Resonance (SPR). The results show that the glucan kinases and phosphatases possess differing abilities to bind glucan substrates. One glucan phosphatase possesses a 50 fold higher affinity for amylopectin than the other, while it only possessed a 3 fold higher affinity for amylose. Both glucan phosphatases showed similar affinities for the short oligosaccharide β -cyclodextrin. We performed structure guided mutagenesis to define the mechanism of these differences. We found that the carbohydrate binding module (CBM) domain provided a stronger binding affinity compared to surface binding sites (SBSs).

EPIGENETIC CHANGES IN THE PROGRESSION OF ALZHEIMER'S DISEASE

Authors

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Abstract

The formation of 5-hydroxymethylcytosine (5hmC), a key intermediate of DNA demethylation, is driven by the ten eleven translocation (TET) family of proteins that oxidize 5-methylcytosine (5mC) to 5hmC. To determine whether methylation/demethylation status is altered during the progression of Alzheimer's disease (AD), levels of TET1, 5mC and subsequent intermediates, including 5hmC, 5-formylcytosine (5fC) and 5-carboxylcytosine (5caC) were quantified in nuclear DNA from the hippocampus/parahippocampal gyrus (HPG) and the cerebellum (CER) of age-matched normal controls, subjects with preclinical AD (PCAD), and late-stage AD (LAD) subjects using immunochemistry. Results show significantly ($P < 0.05$) increased levels of TET1, 5mC, and 5hmC in the HPG of PCAD and LAD subjects. In contrast, levels of 5fC and 5cC were significantly ($P < 0.05$) decreased in the HPG of PCAD and LAD subjects. Overall, the data suggest altered methylation/demethylation patterns in vulnerable brain regions prior to the onset of clinical symptoms in AD suggesting a role in the pathogenesis of the disease.

COTININE, THE PRIMARY METABOLITE OF NICOTINE, ALTERS TRAFFICKING AND ASSEMBLY OF NICOTINIC ACETYLCHOLINE RECEPTORS

Authors

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Abstract

Nicotinic acetylcholine receptors (nAChRs) are pentameric ligand-activated membrane receptors containing alpha ($\alpha 2$ - $\alpha 10$) and beta ($\beta 2$ - $\beta 4$) subunits. Receptor assembly into the correct stoichiometry and composition is necessary for accurate subcellular localization and function. Exposure to nicotine has been shown to alter the trafficking and assembly of nAChRs, resulting in their upregulation on the plasma membrane. Although the mechanism is not fully understood, these changes are believed to contribute to nicotine addiction. We have found that cotinine, the primary metabolite of nicotine, also alters the trafficking, expression, and assembly of nAChRs. We use a pH sensitive fluorophore, super ecliptic pHluorin, to differentiate between intracellular and inserted nAChRs. Similar to nicotine, exposure to cotinine increases the number of $\alpha 4\beta 2$ receptors on the plasma membrane and causes a redistribution of intracellular receptors. In contrast to this, the number of $\alpha 6\beta 2\beta 3$ receptors on the plasma membrane decreases in the presence of cotinine. We also use single molecule photobleaching of green fluorescent protein (GFP) to determine stoichiometry of nAChRs. Cotinine and nicotine both alter the assembly of $\alpha 4\beta 2$ receptors to favor the high sensitivity ($\alpha 4$)₂($\beta 2$)₃ stoichiometry. These results, in combination with its long pharmacological half-life, give cotinine a potential role in the mechanism of nicotine addiction.

SYNTHESIS, FUNCTIONALIZATION, AND APPLICATION OF GRAPHENE QUANTUM DOTS

Authors

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Abstract

Fluorescent carbon nanodots (FCNs) have recently received significant attention because of their attractive characteristics: chemical inertness, biocompatibility and low toxicity. They are considered as promising materials for bioimaging, photocatalysis, sensing, and photovoltaic applications. The confined conjugation of sp²-bonded carbons surrounded by a shell of chemical functional groups can produce bright, photostable, and tunable photoluminescence (PL). While research has been actively conducted to promote brightness and modulate the optical properties of FCNs produced by a variety of synthetic approaches, there is a significant lack of fundamental knowledge about detailed emission mechanism and structure-property-function relation. Our recent progress in controlling the size and chemical functionalities of FCNs will be presented. For the optical characterization of carbon dots, single molecule spectroscopic technique was successfully utilized to unveil complicated photophysics and multi-chromophoric nature of FCNs. Ensemble fluorescence spectra of surface-controlled carbon dots as well as time-dependent fluorescence intensity fluctuation of single carbon dots will be presented.

BIOMOLECULE IMMOBILIZED ELECTRODE SYSTEM TOWARDS ENERGY GENERATION

Authors

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Abstract

Fabrication of bio-electrode systems decorated with redox active biomolecules such as flavins is demonstrated. Flavins, including flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD), and riboflavin (vitamin B), play central roles in many biological electron transfer processes. Depending on the environment such as pH or reduction potential etc. flavins can undergo both two-electron and one-electron reductions. Sufficient stability of the semiquinone intermediate permitted extensive studies of the reductive event. Recently, studies were performed towards one electron oxidation events generating flavinium ions. Flavins undergo interesting photochemistry, as well, thanks to the highly conjugated isoalloxazine ring. Exploiting this additional functionality we sought to study the photoelectrochemical activity of flavin functionalized electrode systems with an effort towards sustainable energy production. As model systems, lumiflavin and FAD were immobilized on carbon electrodes by both drop casting as well as covalent grafting techniques. Activity of these bio-electrodes towards generation of O₂ from H₂O at physiological pH was demonstrated. Irradiation of the electrode system with visible light led to increased activity of the electrodes with at least 3-fold enhancement of oxidation of H₂O. In another effort, generation of photocurrent due to the photo-reduction of the redox-active isoalloxazine ring was studied. Efforts are ongoing to develop Flavoenzyme bound electrode systems for their application in biofuel cells.

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EPIGENETIC MODIFICATIONS IN ALZHEIMER'S DISEASE: REGIONAL AND GENOMIC QUANTIFICATION

Authors

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Abstract

Although epigenetic modifications to cytosine have been extensively studied in embryonic development and cancer, there has been little study of epigenetics as it relates to neurodegeneration, specifically Alzheimer's disease (AD). Studies of global levels of 5-methylcytosine (5-mC) and 5-hydroxymethylcytosine (5-hmC), as well as gene modifications in target brain regions, could provide insight regarding neurodegeneration and dysfunction. To determine global modified cytosine profiles in the brain of AD and control subjects, a GC/MS method was developed and bulk levels of epigenetic modifications were quantified in the superior and middle temporal gyrus (SMTG) and cerebellum (CER) of late stage AD subjects compared to age-matched normal controls (NC). Results show significant differences of 5-mC in the SMTG of AD subjects ($p < 0.05$) compared to NC. To determine if 5-mC oxidation is increased in a target gene associated with AD, q-PCR was used to quantify sequence specific levels of modified cytosine in presenilin-1 (PS1) in nuclear DNA samples isolated from the hippocampus/ parahippocampal gyrus (HPG) of AD and NC subjects. Results show significant alterations in levels of cytosine, 5-mC, and 5-hmC in PS1 of AD subjects compared to NC ($p < 0.05$). Collectively, these studies suggest that epigenetic modifications to cytosine may be associated with AD.

PLASMA TREATED TiO₂ FOR PHOTOCATALYTIC AND SUPERCAPACITOR APPLICATIONS

Authors

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Abstract

In recent years, TiO₂ has gained a strong interest for its potential chemical energy applications for photocatalysis and energy storage. Its low cost, abundant availability, chemical stability, and unique band gap properties make it a very attractive material in these fields. TiO₂ has proven itself to be a powerful photocatalyst; however its wide band gap allows only the absorption of UV light. For solar light to be used as a light source it is critical to expand this absorption to include the visible and IR ranges. In this work, nitrogen containing plasma is utilized to incorporate nitrogen dopants into the lattice of mesoporous TiO₂ films. The incorporation of nitrogen into the film has shown to be an effective way to enhance the visible absorption of the film and thereby greatly increase the catalytic performance in both the UV and visible regions of the spectrum.

In addition to the photocatalysis of nitrogen-doped TiO₂, we also studied the potential application of plasma treated TiO₂ for electrochemical energy-storage devices. TiO₂ demonstrates pseudocapacitance through redox reactions which take place at its surface. Nanostructured TiO₂ is utilized to provide a large surface area which increases the amount of reactions which can take place in a given area. However, pristine TiO₂ suffers from low electrical conductivity which lowers both its specific capacitance and power density. In this work, hydrogen plasma is used to create oxygen vacancies and introduce surface hydroxyl groups which allow for greater conductivity and greatly improves electrochemical capacitance behavior.

APPLICATION OF CELL-DERIVED VESICLES IN SINGLE-MOLECULE STUDIES

Authors

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Abstract

Single molecule studies are primarily limited to proteins that can be purified and solubilized outside of the cellular environment. For membrane receptors this is usually achieved by employing surface acting agents. However, these techniques are not applicable to many types of membrane receptors. These complex proteins often consist of multiple subunits and require the presence of a lipid bilayer to maintain function and structural integrity. Both are lost in a detergent environment. We isolated transmembrane proteins such as the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), nicotinic receptors, and epidermal growth factor receptors into cell derived vesicles for single molecule studies. Isolating receptors in vesicles keeps the protein intact in a native cellular membrane. Receptors contained in vesicles were isolated on the surface of a glass substrate to determine their stoichiometry. We found that $\alpha 3\beta 4$ was predominately present with a $(\alpha 3)_2(\beta 4)_3$ stoichiometry. The stoichiometry of $\alpha 3\beta 4$ was validated employing a dual-color single molecule experiment within the same vesicle. We also showed that single molecule studies of vesicles can be extended to solution based applications. Binding of epidermal growth factor (EGF) to vesicles containing epidermal growth factor receptors (EGFRs) was observed using fluorescence correlation spectroscopy (FCS). We believe these methods will extend single molecule studies to previously inaccessible transmembrane proteins.

EFFECT OF MUTATIONS AND UNNATURAL SUBSTRATES ON THE STABILITY OF P450 BM3 AS DETERMINED BY CHEMICAL AND THERMAL DENATURATION

Authors

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Abstract

Cytochrome P450s are a family of proteins capable of carrying out reactions such as hydroxylation, epoxidation, and halogenation on several classes of substrates. Most of the human P450s are membrane bound, making them difficult to study in vitro. As an alternative, P450BM3, a bacterial protein, can be used as a model system. A promiscuous P450BM3 created by point mutations is able to catalyze a wider range of reactions than the wild-type. Studying the stability and dynamics of these mutations in the presence of unnatural substrates enhances our understanding of the relationship between substrate choice and stability. In this work, we use two techniques to investigate P450BM3 with and without bound substrates: pulse proteolysis and the N-{4-(7-diethylamino-4-methyl-3-coumarinyl) phenyl}maleimide (CPM) assay. Pulse proteolysis examines proteolytic susceptibility of the protein due to chemical denaturation. The CPM assay monitors fluorescence of a thiol-specific fluorophore (CPM) reacting with solvent-exposed cysteines as a result of thermal denaturation. These two assays provide a novel way to assess the stability of P450s. Preliminary results suggest that there is trade-off between stability and promiscuity, and that there is an optimal compromise that allows for catalytic function.

CLONING AND PARTIAL CHARACTERIZATION OF A NITROREDUCTASE FROM THERMUS THERMOPHILUS: RECENT EFFORTS TOWARD REDOX TUNING

Authors

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Abstract

A nitroreductase (NR) homologue, NADH oxidase (NADOX), from the extremophile *Thermus thermophilus* may share the large substrate repertoire known for many NR flavoenzymes but has been much less studied. We propose that NADOX is able to perform much of the same chemistry as NR but across a broader range of pH, temperature, and chaotropic agent concentrations. Further, we hypothesize that the extreme stability of NADOX should allow the enzyme to be more tolerant of mutations compared to NR and thus better suited for protein design.

We seek to alter the two-electron chemistry of NADOX with the aim of designing an active site capable of accepting reducing equivalents sequentially from an electron transfer chain. Once fully reduced, the designed NADOX could be capable of donating electron pairs to form covalent bonds. If successful, the thermostable enzyme would find application in bridging photo-driven charge separation devices (one-electron transfer chains) with chemical energy storage (two-electron covalent bonds).

Progress to date includes the subcloning of the NADOX gene, purification of wild type and mutant holoenzymes, as well as initial characterization of catalytic activity and redox properties.

OZONOLYSIS OF CATECHOL AT THE GAS-SOLID INTERFACE

Authors

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Abstract

The diverse sources, complex chemical composition, and transformations that atmospheric aerosols undergo have a direct impact on Earth's climate, regional visibility, and public health. Field observations have suggested that α -dicarbonyls, keto- and di-carboxylic acids present in rural aerosols from biomass burning are more abundant than in polluted urban areas. We have proposed a mechanism to account for the previous observations based on studies of the oxidation of catechol, a proxy of biomass burning species at the air-water interface. While 10-25 ppmv ozone competes with in situ produced hydroxyl radicals for catechol at the air-water interface, thin solid films ($< 1 \mu\text{m}$) of catechol are converted into organic acids under variable relative humidity (RH = 0-85%). Product identification is performed by ion chromatography-mass spectrometry supplemented by infrared monitoring of $\nu(\text{C}=\text{O})$ and $\nu(\text{O}-\text{H})$ peaks at 1680 cm^{-1} and 3400 cm^{-1} , respectively. The rate of catechol loss increases exponentially with increasing RH. Characterization of thin films by atomic force microscopy allowed the estimation of ozone uptake by catechol. These observations suggest that water plays a key role in heterogeneous chemistry on the surfaces of aerosols.

FERROCENE-FUSED HETEROCYCLIC SYSTEMS

Authors

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Abstract

Thiophene-based polymers have evolved as some of the most successful materials for organic electronic applications. The structural variation of oligo- and polythiophenes allows a broad electronic and chemical tuning range. Our project aims to study electronic, electrochromic, redox, and optical properties of thiophene-based materials integrated with organometallic systems such as ferrocene. We begin by converting 1,2-bis(hydroxymethyl)ferrocene to 1,2-bis(thiuroniummethyl)ferrocene with thiourea under acidic conditions. Refluxing the salt in base followed by acidification results in 1,2-bis(mercaptomethyl)ferrocene, which is oxidized to the cyclic 1,4-dihydro-2,3-ferrocenodithiin. Ring contraction of the cyclic dithiin gives the thioether, 1,3-dihydroferroceno[c]thiophene. Periodate oxidation gives 1,3-dihydroferroceno[c]thiophene-2-oxide (1), a potential precursor for ferroceno[c]thiophene via Pummerer dehydration. Dehydration of 1 and in situ trapping of the resulting thiophene are under study. Besides the sulfur system, we have also been looking into synthetic routes to ferrocene-fused furan and ferrocene-fused pyrrole. Recent renewed interest into α -oligofurans for organic electronics encourages investigation into these heteroatom systems as well.

SYNTHESIS AND CHARACTERIZATION OF FERROCENE-FUSED TROPONES, THIOTROPONES AND TROPONE OXIMES

Authors

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Abstract

We are interested in potential applications of metallocene-fused tropones and derivatives as organic electronic materials. Condensation of 1,2-diformylferrocene with acetone or 1,3-diphenylacetone in the presence of KOH leads to the ferrocene-fused tropone (η^5 -2,4-cyclopentadien-1-yl)[(1,2,3,3a,8a- η)-1,6-dihydro-6-oxo-1-azulenyl]iron and its 5,7-diphenyl derivative [figure1], E = O, as previously reported by Tirouflet. In the presence of piperidine, 1,2-diformylferrocene and 1,3-diphenylacetone gives the Michael addition of piperidine to the tropone. Lawesson's reagent converts the ferrocene-fused tropones to thiotropones (1, E = S) or detached azulenethiols (2, E = S). Reactions of the ferrocene-fused thiotropones with hydroxylamine give the corresponding oximes (1, E = NOH). Products are characterized by using spectroscopic methods and X-ray crystallography. Their electronic properties are studied by using cyclic voltammetry and UV-visible spectroscopy.

A HIGH THROUGHPUT SCREENING APPROACH TO IDENTIFY SELECTIVE RU(II) AGENTS FOR THERAPEUTICALLY RELEVANT DNA SEQUENCES

Authors

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Abstract

Non-canonical DNA structures are prevalent in cancer, and accordingly are potential targets for drugs and diagnostic agents. G-quadruplexes are commonly found in telomeres and promoter regions of proto-oncogenes such as c-myc, c-kit⁺ and bcl-2. DNA damage sites, such as mismatches, bulges, or abasic sites, are prominent in cancer cells due to deficiencies in DNA repair mechanisms. Luminescent ruthenium(II) polypyridyl complexes can be used to detect these structures, as they preferential binding to G-quadruplexes and DNA damage sites, and act as luminescent “light switches” when bound to the DNA. Incorporation of strain transforms these photophysical “light switches” into photochemical “light switches” that are capable of chemically reacting with DNA upon intercalation. We have synthesized a variety of Ru(II) polypyridyl complexes and screened them against an array of 32 different biomolecules, focusing on different DNA sequence and tertiary structure. Slight chemical modifications to the intercalating ligand structure yielded differences in the ability of the complexes to discriminate between the types of DNA.

CHARACTERIZATION OF *S. AUREUS* FAMILY II PYROPHOSPHATASE PPAc AND THE FUNCTIONAL RELEVANCE OF DIMERIZATION

Authors

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Abstract

Inorganic pyrophosphatase (PPase) catalyzes the hydrolysis of pyrophosphate, which provides energy for many cellular processes. Based on sequence homology, PpaC from *Staphylococcus aureus* has been identified as an inorganic PPase. Here, we recombinantly expressed and purified PpaC in its active form from *Escherichia coli*. We found that consistent with other family II PPases, PpaC from *S. aureus* 1) preferred Mn^{2+} for activity; 2) catalyzed the hydrolysis of pyrophosphate but not ATP; and 3) existed as a dimer. Metal binding is critical for the function of family II PPases and has been shown to drive dimerization. To elucidate the functional role of dimerization, we introduced several point mutations at the dimer interface to decouple dimerization from metal binding. The dimer interface is distant from the active site. Therefore, mutations at the dimer interface are not likely to directly affect substrate binding. Two mutants were identified, Y111S and R99M, that existed predominantly as monomers when purified. Both mutants still bound Mn^{2+} but completely lost their catalytic activity. These results suggest that dimerization was not merely a passive consequence of metal binding, but rather a critical activation process for family II PPase activity. In addition, unlike most known metalloenzymes, metal binding did not increase the thermal stability of PpaC. PpaC adopted completely different unfolded states when thermally denatured in the presence and absence of metal ions.

CATALYTIC DEOXYGENATION OF TRISTEARIN TO HYDROCARBONS OVER SUPPORTED NICKEL ALLOY CATALYSTS

Authors

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Abstract

The oxygen content of the fatty acid methyl esters that constitute biodiesel is responsible for a number of shortcomings with respect to its fuel properties. Consequently, there is considerable interest in the development of deoxygenation processes for the conversion of lipid feeds to drop-in hydrocarbon fuels. The removal of oxygen from fats and oils via decarboxylation/decarbonylation (deCOx) is particularly attractive due to the fact that this approach does not require the high H₂ pressures or problematic sulfide catalysts used in hydrodeoxygenation, the process most commonly used to convert lipids to hydrocarbons. We have previously demonstrated that oxide-supported Ni catalysts exhibit good activity for the deCOx of both model and realistic lipid feeds, while also being inexpensive and recyclable. However, the selectivity and the resistance to deactivation of these Ni catalysts must be improved. The present study aimed at achieving these goals through the use of Cu or Sn as promoters. Notably, in catalyst screening work performed in semi-batch mode using tristearin as a model lipid feed, a Cu-promoted catalyst exhibited increased conversion and selectivity to diesel-range hydrocarbons when compared to a Ni-only formulation at 260 °C, a Sn-promoted catalyst showing the best performance when the same reaction was essayed at 350 °C. Tellingly, the temperature programmed reduction of the catalysts tested showed that the Cu-promoted catalysts had lower reduction temperatures than the monometallic Ni catalyst, which suggests that the promotion effects observed for the Cu promoted catalysts can be explained by the ability of Cu to improve the reducibility of Ni.

CATALYTIC CONVERSION OF MONOSACCHARIDES INTO 5-(HYDROXYMETHYL)FURFURAL USING ALUMINUM COMPLEXES SUPPORTED BY BIDENTATE PHENOXY-A

Authors

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Abstract

Several dimethyl aluminum complexes containing bidentate phenoxy-amine ligands were synthesized, identified by spectroscopic techniques, and their structures determined by X-ray crystallography. Preliminary studies of the potential of these complexes as catalysts for the dehydration of glucose and fructose to 5-hydroxymethylfurfural (HMF) in ionic liquids have been carried out; HMF was obtained in moderate yields. Variation of the amino group substituent was found to have crucial influence on reactivity of the aluminum complexes, presumably due to changes in steric and electronic properties of the catalysts. This poster presentation will discuss some of our findings.

AROMATIC HETEROCYCLES FOR OPTIMIZATION OF ENERGY STORAGE SYSTEMS

Authors

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Abstract

Lithium-ion batteries (LIBs) are a preferred power source for portable electronics, while redox flow batteries (RFBs) present an opportunity for large-scale stationary energy storage. Materials optimization has brought about substantial improvements in LIBs as well as the development of the aqueous all-vanadium RFB system, but there remain limitations to the efficiency and safety of these devices. LIBs suffer from overcharge – a harmful condition which limits battery lifetimes and can lead to increased internal pressure and thermal runaway, thence to smoking and/or fire. The aforementioned vanadium RFB system is the most advanced yet under consideration, but the voltage window is limited and components are often extremely corrosive. Aromatic heterocycles may constitute a solution to both of the above limitations – as redox shuttles to protect against overcharge in LIBs and as organic electrolyte materials in non-aqueous RFBs. This research utilizes computational and experimental prescreening/design techniques to identify promising compounds for use in LIBs and RFBs, thereby reducing the amount of time (and money) lost in synthesizing and cycling incompatible compounds. It furthermore encompasses the synthesis and incorporation of said compounds into battery systems to determine the validity of our prescreening techniques, as well as the performance of each compound in real-life systems.

SMALL MOLECULE INDUCED CHANGES IN THE TRAFFICKING OF THE CYSTIC FIBROSIS CONDUCTANCE REGULATOR

Authors

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Abstract

Cystic Fibrosis (CF) is a recessive genetic disease caused by any one of more than 1000 unique mutations to the gene which codes the cystic fibrosis transmembrane conductance regulator (CFTR). These mutations result in dysfunction of CFTR from either trafficking or functional deficits. Defective CFTR causes a decrease in CFTR chloride channel function and accumulation of viscous mucus at the surface of lungs, pancreas, gut and testes, resulting in blockage, infection, inflammation and finally organ failure. About 70% of Cystic Fibrosis is caused by the deletion of phenylalanine at position 508 in CFTR (ΔF 508-CFTR). The one amino acid deletion causes immature CFTR to be degraded in the endoplasmic reticulum (ER), which means CFTR trafficking to plasma membrane fails. My current work focuses on how the chemical chaperone (VX-809) alters the trafficking of CFTR to the plasma membrane. We utilize a pH sensitive fluorophore, super ecliptic phluorin (SEP), to differentiate between CFTR in the ER and on the plasma membrane (PM). In this way, the relative percentage of receptors on the plasma membrane compared to the peripheral endoplasmic reticulum can be determined and individual insertion events of a single vesicle arriving at the plasma membrane can be counted. We have found that there is an increase in the percent of receptors on plasma membrane when ΔF 508-CFTR is exposed to the chemical chaperone (VX-809).

OXIDATIVE DAMAGE TO DNA IN PACKAGED AND UNPACKAGED STATE

Authors

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Abstract

In sperm chromatin, the general consensus is that tight packing of DNA in sperm nuclei is necessary to limit DNA damage due to free radicals since DNA repair is absent in mature sperm. The replacement of histones with protamines in late-stage spermatogenesis is assumed necessary to accomplish sufficient DNA stability. Sperm DNA damage is especially vulnerable to oxidative stress and correlates not only to infertility but also impacts normal embryonic development. This damage is currently poorly characterized, but is known to involve hypomethylation of key genes, oxidative base damage, endonuclease-mediated cleavage and the formation of adducts with xenobiotics and the products of lipid peroxidation. From previous work on understanding the resulting structural packaging in polycation-DNA systems, we have a convenient means to directly assess the role of packing on free radical access and DNA damage in protamine-DNA. Accessibility is not only matter of sterics but also physical chemical interactions. Here, we show gel electrophoresis results of the damage induced on packaged and unpackaged DNA by two different free radical sources as studied by gel electrophoresis. Our initial results suggest even small changes in DNA packaging result in significant differences in free radical accessibility to the DNA helices. Our long-term goal is to determine quantitatively the interrelationship between DNA packaging densities and the resulting accessibility of DNA to reactive oxygen species (ROS).