ChemE In-house Symposium

May 30, 2019

Department of Chemical Engineering,
Indian Institute of Science (IISc), Bangalore

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WELCOME

Welcome to the 2019 Annual Chemical Engineering Symposium at the Indian Institute of Science. This event is primarily meant to highlight the cutting-edge research being conducted by students and research staff of the Chemical Engineering Department, and is in continuance of a long tradition in the department.

The 2019 Annual Chemical Engineering Symposium is jointly organized by the Chemical Engineering Association (CEA) and the Chemical Engineering Department. We thank the Chairman of the department, Prof. Ganapathy Ayappa, who is a constant source of inspiration and support to CEA.

We have an exciting line-up of presentations this year. These presentations demonstrate the diversity of research being conducted in the department and include areas like rheology, molecular dynamics, catalysis, energy storage, biological systems engineering and medical diagnostics, among others. The event will feature 10 oral presentations and 16 poster presentations from our students. Dr. Janhavi Raut from Hindustan Unilever Limited will deliver the keynote lecture on the topic of microbial assemblies and associated challenges. Dr. Narendra Dixit , will represent our faculty and deliver a lecture on engineering the germinal center reaction.

Every year, this symposium is enthusiastically attended by several of the department's alumni. We anticipate several of our alumni from industry to be present this year as well, which will create excellent networking opportunities. This is also a wonderful opportunity for our students to learn about all the exciting research happening within the department and I hope that this will lead to fruitful collaborations.

Finally, it would be remiss of me not to mention the efforts of all student members of CEA, who have worked hard to make this event a success.

I really hope that you enjoy this event…

Bhushan J. Toley
President
Chemical Engineering Association

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Technical Program

Block	Start Time	Speaker	Type	Topic
Snacks	08:45	Coffee		
Session 1	08:55	Chairman's Address		
	09:00	Md. Aslam	Student 1	Harnessing natural convection in membrane-less soluble lead redox flow batteries
	09:15	C. Dinesh	Student 2	Self assembly of nanoparticles for catalyst design
	09:30	Madhavan	Student 3	Inkjet printed strain sensors towards electronic wearables
	09:45	Bhanupriya Boruah	Student 4	Enhanced Photocatalysis and Bacterio-inhibition in Nb_2O_5 via Versatile Doping of Metal (Sr, Y, Zr, Ag)
Poster 1	10:00	Photo Session		
	10:15	Poster Session and Tea break		
Session 2	**11:45**	**Janhavi Raut**	**Keynote**	**Microbial Assemblies: Exciting Challenges for Chemical Engineers**
	12:30	Aashish Gupta	Student 5	On the flow of grains through a screw conveyor
	12:45	Priyanka V	Student 7	Digital droplet amplification for nucleic acid quantification
	13:00	Md. Tabish	Student 6	Shear thickening of Non-Brownian suspensions
Lunch	13:15	Lunch		
Session 3	**14:15**	**N. Dixit**	**Faculty Talk**	**Engineering the germinal center reaction**
	15:00	Navjot Kaur	Student 8	A modular paper and plastic microfluidic device for next generation tuberculosis diagnosis
	15:15	Pradyumn Sharma	Student 9	Molecular Dynamics Investigation of Small Molecule Interactions with Bacterial Cell Membranes
	15:30	N. Sathishkumar	Student 10	A transport-reaction model for expanding the dynamic range of lateral flow immunoassays using real-time imaging
Poster 2	15:45	Poster Session and Tea break		
Conclusion	17:15	Prizes		
	17:25	B. Toley	Vote of Thanks	

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Poster Session I

P1	Aamir Faisal	High-order interactions can eclipse pairwise interactions in shaping the structure of microbial communities
P2	Aashish Thakur	Enhancing the cycle life of soluble lead redox flow battery (SLRFB)
P3	Shruti Soni	Measurement of glucose levels in human saliva using a disposable paper test strip
P4	Ananya Saha	Modelling virological breakthrough due to resistance to antibodies during treatment interruption suggests avenues for prolonging HIV-1 remission
P5	Aadhil Basith A	Modelling flow through coronary arteries
P6	Sagar Bathla	Molecular dynamics of water molecules translocating through graphene nanopores
P7	Shivam Gupta	Molecular dynamics simulation of Drug molecule translocating through efflux pump
P8	Ratnasri K.	Heterogeneity in arabinose operon gene expression in bacteria

Poster Session II

P9	Peter V.Dsouza	Rheology of Cohesive Granular powders
P10	Shivanand Kumar Veesam	Molecular Modeling of Gas Hydrates
P11	Satyaghosh Maurya	Single particle tracking to probe membrane protein/peptide interactions
P12	Suraj Jagtap	Dengue virus diversity revealed by clinical metagenomics
P13	Sreepadmanabh M, and Kavyashree Rai	Simulating the effect of flow and trajectory dynamics on metastatic ovarian cancer cells and their multicellular collectives
P14	Andrea Dsouza, and Saylee Jangam	A large-volume sputum collection and dry-storage device for tuberculosis molecular diagnostic testing
P15	Ananthu James	Attenuation of HIV replication fitness among men who have sex with men (MSM)
P16	Ketan Ganar	Visual detection of SNP using molecular beacon for detection of first line drug resistant tuberculosis

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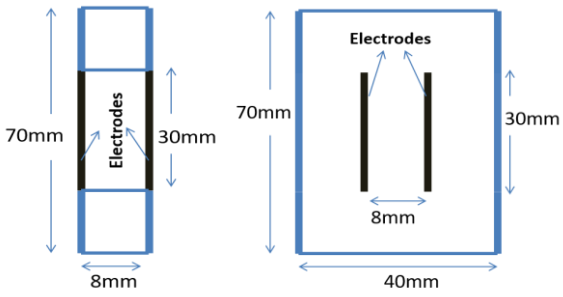
ORAL PRESENTATION ABSTRACTS

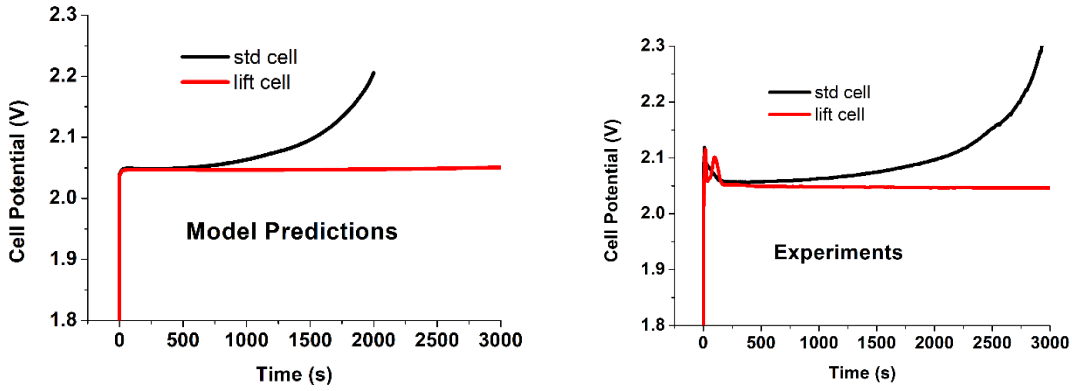
Harnessing natural convection in membrane-less soluble lead redox flow batteries

Md Aslam Ansari and Sanjeev Kumar

Harvesting of renewable energy requires efficient energy storage systems. Rechargeable flow batteries offer certain advantages over other energy storage techniques in use, such as lifting of water, compression of air, flywheel, etc. In a flow battery, electrolyte flowing through/between the two electrodes, electrical energy is stored as chemical energy through reversible redox electrochemical reactions. Typical applications of large-scale storage include load-leveling, peak shaving, backup power, electric vehicles, etc. While some flow cells have been scaled up, we still need to develop flow batteries with high energy and power densities, large cycle life, and low cost.

Soluble lead redox flow battery (SLRFB) is among the least expensive in its class, because of the raw material used and the single electrolyte flow loop which eliminates the expensive proton exchange membrane. Challenges such as limited cycle life and low energy efficiency need to be overcome, however, to take it to the next label. In our research group, we have established through CFD-electrochemical reaction modeling, measurements, and flow visualization the dominant role of natural convection in SLRFB. In this work, we present our efforts to harness natural convection for efficient battery designs that need minimal mixing during relaxation between charge-discharge cycles. A detail investigation of natural convection has been done in standard (on wall electrodes design) and lift (off wall electrodes design) cells shown schematically in the right figure. This shows great promises to the energy storage applications. We have also investigated the cell performance at low external electrolyte flow rate in the presence of natural convection. This shows that cell can be charge-discharge at constant potential even at very low electrolyte flow rate in the presence of natural convection.





The figure above shows the model validation for charge performance in standard and lift cell design for natural convection case.

Self-assembly of nanoparticles for catalyst design

C Dinesh and S Punnathanam

Self-assembly is a process in which components, spontaneously form stable, well-shaped, ordered aggregates. Catalysts play a prominent role in reducing energy footprint in many industrial processes by minimizing the extreme conditions required for chemical reactions. Catalysts can be improved by controlling their structure. Since catalysts need large surface area and large pores for diffusion of reactants and products, controlling the structure is important for improving of their performance. To this end, development of open structured catalysts has relevance to chemical process industries. Open structures are those in which the microscopic constituents occupy only a low fraction of the total volume leaving open space between them. The key element in generating open crystal lattices is inducing directional pair interactions between nanoparticles during their self-assembly [1]. In this regard, Jabes et al. [2] has shown a possible source of anisotropy between ligand coated spherical nanoparticles. They showed that even when the time-averaged structure of the ligand shell is spherical, fluctuations in ligand density will leads to deviations in spherical symmetry, which in turn results in anisotropic interactions between spherical nanoparticles. They also highlighted the many-body nature of ligand shell on interparticle interactions. Previous computational studies of self-assembly have neglected this multi-body interactions. In this study, we wanted to see multi-body effect between spherical nanoparticles towards self-assembly of crystalline aggregates. We plan to study effect of multi-body effect on interactions between nanoparticles by using potential of mean force calculations. Gold nanoparticle coated with self-assembled monolayer of dodecane thiol is the system selected to study multi body interactions. Once the enough data is generated by simulations, the goal is to model the interactions between group of particles.

References:

1. Szilard N. Fezer and David J. Wales, Soft Matter. 11, 6663-6668 (2015)

2. B. S. Jabes, H. O. S. Yadav, S. K. Kumar, and C. Chakravarty, J. Chem. Phys. 141, 154904 (2014)

Inkjet printed strain sensors towards electronic wearables

R Madhavan, and S Venugopal

In recent years, wearable electronics has garnered widespread attention due to their flexible, stretchable and elastic nature. Typically, "wearable electronics" monitor signals in a continuous manner from the sensed surface on which the device is placed. The use of elastomers or other unconventional materials as base substrates render them functional in terms of being light in weight and enabling conformal contact on curved and soft surfaces. The materials such as metal nanoparticles, graphene, carbon nanotubes, etc., have been utilized as functional sensing elements due to their impressive electrical and mechanical properties. The use of silver nanoparticles along with flexible and stretchable substrates has been widely utilized to fabricate wearable devices through various fabrication methods.

Conventional fabrication methods for wearable electronics include vacuum deposition, electroless plating, and photolithography, but these methods suffer from limitations such as high equipment costs, multi-staged procedures and production of environmentally undesirable wastes in large quantities. To foster effective and scalable electronic manufacturing, alternative methods include inkjet printing, flexographic printing, gravure printing, screen printing and roll to roll printing. Inkjet printing is a low-cost method for fabricating wearable electronic devices. It generates a functional arrangement in a non-impact, maskless and additive manner. This research work describes the design and development of flexible and stretchable wearable strain sensors by an inkjet printing process through a novel print, expose and develop process based on silver halide photography for silver-based nanomaterials

Enhanced photocatalysis and bacterio-inhibition in Nb_2O_5 via versatile doping of metal (Sr,Y,Zr,Ag)

Bhanupriya Boruah, J Modak and G Madras

Unique optical properties render the semiconductor Nb2O5 nanoparticles suitable for light harvesting and photocatalytic applications. This study focuses on determining the optical properties such as band gap, conduction band edge, valence band edge and the work function of as-prepared solution combustion synthesized Nb2O5 nanoparticles with the help of UV-Vis Diffused Reflectance spectroscopy (DRS) and Ultraviolet photoelectron spectroscopy (UPS) techniques. Phase purity and the oxidation states of the elements present in the material were confirmed from X-ray Diffraction (XRD) patterns and X-ray photoelectron spectroscopy (XPS), respectively. Doping semiconductors with different metal ions impact the activity of the material, and therefore efforts were made to understand the effect on the photocatalytic performance of Nb2O5 due to the incorporation of metal dopants viz Sr, Y, Zr, and Ag. Parameters which are closely related to the photoactivity of the catalysts such as presence of surface defects, oxygen vacancies, surface area, charge carrier dynamics were determined from Photoluminescence (PL) analysis, Brunauer Emmett Teller (BET) surface area measurements and Time-resolved fluorescence (TRF) analysis respectively. In addition, the dopant concentrations were optimised for enhanced photocatalytic activity. The doped Nb2O5 nanoparticles showed significant activity towards targeted degradation of organic pollutants 2-chlorophenol (2-CP) and dye contaminant methylene blue (MB). This strategy yielded a robust response towards inactivation of E.coli microorganism as well. Adsorption and photodegradation of MB followed Lagergren's pseudo 1st order reaction model and Langmuir Hinshelwood model respectively. Bacteria inactivation and 2-CP photodegradation followed 1st order kinetics. Reusability of the catalyst for 5 cycles was demonstrated. Finally, a plausible mechanism is proposed based on radical trapping experiments and combined analysis of the characterization techniques.

On the flow of grains through a screw conveyor

Aashish Gupta and P R Nott

Screw conveyors are widely employed in industries for the bulk transport of powdered substances. Past studies have tried to correlate the discharge rate through the conveyors with the angular velocity of the screw shaft. But an understanding of the actual flow profile can assist in better designing of the screw conveyors. In the current work, we have employed DEM (Discrete element method), a particle-scale numerical method, to simulate the bulk flow inside a screw conveyor. The azimuthal velocity field in the cross-sectional plane of the conveyor shows a major chunk of material exhibiting solid body rotation. The axial velocity does not seem to vary much throughout the cross-section.

A simple model, that assumes the entire granular media as a single rigid body sliding past the screw flight with the screw rotation, has been proposed. Linear and angular momentum balances have been applied to a suitably chosen continuum element. The equations have been further simplified in the limit of the friction coefficient on the screw surface tending to zero. Maximum possible axial velocity for a given angular velocity and geometry of the screw is finally obtained. For maximum discharge, the screw geometry can be optimized by setting the pitch to casing diameter ratio to an interesting number.

Digital droplet amplification for nucleic acid quantification

Priyanka V and Rahul Roy

Nucleic acid amplification based 'quantitative Polymerase Chain Reaction' (qPCR) remains the gold standard for nucleic acid quantification in clinical diagnostics. As an alternative, droplet digital PCR provides absolute quantification of nucleic acids without the requirement for calibrations and reference controls. Despite its advantages, it suffers from limitations of thermal cycling at elevated temperatures and requirement of separate platforms for droplet generation, nucleic acid amplification and signal detection.

Here, we report an integrated droplet digital isothermal Nucleic Acid Quantification (ddiNAQ) platform that enables facile, accurate and absolute nucleic acid quantification. Incorporation of isothermal Recombinase Polymerase Amplification (RPA) provides fast amplification (~25 mins to cross detection threshold for single molecules with DNA intercalating dyes) within monodisperse droplets with the flexibility of all operations in a single device. We benchmarked ddiNAQ against ddPCR and demonstrate comparable performance. By monitoring real-time digital RPA reactions, we evaluate the role of various parameters on amplification efficiency, speed and non-specific amplification.

Shear Thickening of granular suspensions

Md Tabish and P R Nott

The phenomenon of shear thickening has received a lot of attention in last few years and is now believed to be friction generated interparticle contact network, resulting in tremendous increase in viscosity at critical shear stress. A common feature of experimental studies is that the suspension is first pre sheared, mostly for an hour or so before shear rate/shear stress sweep experiments are performed. However, little is known about what happens during it, and why is it important. Here we present that pre shear holds the key in obtaining DST and show the evolution from continuous shear thickening, to DST and then to shear jamming where the suspensions creeps like granular material at higher stress. Also, shear cyclic experiments on shear thickened states yield that the strain required to undergo jamming is much larger than what the theories suggest and provide plausible arguments to explain it.

Engineering the germinal center reaction

Narendra Dixit (Faculty Talk)

We fight infections by producing proteins called antibodies, which bind to and target pathogens for degradation. The structure of antibodies has to be tuned to recognize specific pathogens with high affinity for the immune response to be effective. This tuning happens in regions called the germinal centers in our bodies and the process is called the germinal center reaction. Interest in the germinal center reaction has grown in recent times because of its centrality to the fight against HIV. It turns out that only a few rare individuals manage to produce potent antibodies against HIV, and that too in inadequate quantities and after much delay. Can the production of these potent antibodies be expedited and quantities increased? This problem has parallels to the classic problem of improving the speed, selectivity, and the yield of reactions that we often encounter in chemical processes. I will present in this talk recent work from our group where we employed stochastic simulations of the germinal center reaction to unravel trade-offs that limit the germinal center output and suggest personalized strategies of intervention for maximizing the output.

A modular paper and plastic microfluidic device for next generation tuberculosis diagnosis

Navjot Kaur and Bhushan Toley

Most of the DNA-based tuberculosis (TB) diagnostics available today are confined to sophisticated labs, highly dependent on resources and trained users. Access and affordability of these diagnostic solutions are huge obstacles for their mass employment, limiting their benefits. A paper and plastic-based diagnostic tool has been developed to address these challenges and enable rapid, inexpensive and point-of-care-compatible nucleic acid amplification tests (NAATs) for the detection of TB. The prototype, coined 'FLIPP-NAAT' (Fluorescent isothermal paper-and-plastic NAAT), works on the principles of isothermal DNA amplification and fluorescence-based DNA detection. Concentrated efforts have been made to enable a simple user experience, independent of any specialized training. The only ancillary equipment required for testing in FLIPP-NAAT is a regular laboratory incubator and the results can be captured using a cell-phone camera. The material cost of making the device is INR62 and the reagent cost per reaction zone is INR41 only. The device has been designed to incorporate respective positive and negative controls to increase the reliability of the test results. The device design is modular as the number of reaction zones can be changed depending on the requirement, making it suitable for high throughput testing. The loop-mediated isothermal amplification (LAMP) assay used for DNA amplification in FLIPP-NAAT demonstrated high specificity to Mycobacterium tuberculosis (Mtb), sensitivity of the order of 10 copies of Mtb genomic DNA, and tolerance to foreign DNA and viscous sputum samples. These results are very promising in terms of considering FLIPP-NAAT as a potential replacement for smear microscopy at peripheral laboratories at a significantly lower (material and labor) cost and a marked improvement in sensitivity for an initial screening of patients. Although demonstrated for the detection of TB, FLIPP-NAAT is a platform technology that can be used for amplification of any nucleic acid sequence from any sample type using appropriate sample preparation. Future work is focused on stabilizing dry-storage of reagents in FLIPP-NAAT to make the device amenable to storage and transportation without cold chains.

Molecular Dynamics Investigation of Small Molecule Interactions with Bacterial Cell Membranes

Pradyumn Sharma and K. G Ayappa

The bacterial cell envelope is a complex multi-layered structure that has evolved to protect these organisms from their unpredictable and often hostile environment. An understanding of the molecular basis for transport and interaction of antibacterial molecules with the bacterial cell envelope will enhance our understanding of combating bacterial infections and resistance. Here we used all-atom and coarse-grained simulations to investigate the interaction of thymol, an antibacterial monoterpene phenol found in the essential oils extracted from plants with a model of the inner membrane and outer membrane of Escherichia coli, an archetypical Gram-negative bacterium. Molecular dynamics simulations have been carried out using both all-atom and coarse-grained descriptions for thymol and the membrane. Our results indicate that thymol spontaneously enters the bilayer and positioning themselves below the lipid headgroups. Potential of mean force computations indicate that insertion of thymol into the membrane is thermodynamically favourable. Also, we have looked at the effect of lipid composition in inner membrane on the insertion of these molecules. Our results suggest that it requires proper modelling of bacterial cell membrane morphology to understand these interactions.

A transport-reaction model for expanding the dynamic range of lateral flow immunoassays using real-time imaging

Sathishkumar N, and Bhushan J. Toley

The dynamic range of LFIA's is limited by the 'hook effect', according to which, test line signal intensities reduce with increasing analyte concentration beyond a threshold analyte concentration. It has been shown experimentally that the hook effect may be mitigated by real-time imaging of test and control lines[1], but till date there are no mathematical models that explain this phenomenon. While several transport-reaction models have been developed to predict test line intensities as a function of analyte concentration[2], we present the first transport-reaction model of real-time signal generation in the test and control lines of lateral flow immunoassays (LFIA). This model provides theoretical underpinnings of how the dynamic range of an LFIA may be expanded by real-time imaging.

References:

[1] E. Rey, D. O. Dell, S. Mehta, and D. Erickson, "Mitigating the hook effect in lateral flow sandwich immunoassays using real- time reaction kinetics," pp. 3–6.

[2] S. Qian and H. H. Bau, "A mathematical model of lateral flow bioreactions applied to sandwich assays," vol. 322, pp. 89–98, 2003.

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POSTER PRESENTATION ABSTRACTS

High-order interactions can eclipse pairwise interactions in shaping the structure of microbial communities

Aamir Faisal and Narendra Dixit

Microbial species exhibit sophisticated interdependencies as strategies to coexist in communities. Unraveling these interdependencies would help engineer natural and synthetic microbial communities, of importance to food and healthcare applications. Here, we constructed a synthetic microbial community of 7 naturally co-occurring oral bacteria and employed a bottom-up approach to understand the role of interspecies interactions in deciding the structure of this community. The community showed strong evidence of high order interactions. The abundance of the species Actinomyces viscosus was high alone, low in the presence of any but not all of the other species, and high again in the 7-species community. To understand these interactions, we investigated the influence of the other species individually and in combination on Actinomyces viscosus. The species individually either suppressed or remained independent of Actinomyces viscosus. These binary interactions captured the observations of all 3-, 4-, 5- and 6-species communities involving Actinomyces viscosus that we studied, suggesting that no lower order interactions could explain the increase in the Actinomyces viscosus abundance in the 7-species community. The 7-species community structure was thus due to 7th order interactions that eclipsed the pairwise interactions. We employed a generalized Lotka-Volterra model to quantify these interactions. The interactions captured the structure of a new community containing the 7-species above and an additional species, validating the model and presenting a handle to tune the community structure. Overall, our study demonstrates the existence of high order interactions that could be critical to the structure of multi-species microbial communities.

Enhancing the cycle life of soluble lead redox flow battery (SLRFB)

Aashish Thakur and Sanjeev Kumar

The integration of renewable energy sources like wind, solar, tidal etc. into the grid supply, to supplement the conventional energy supply, requires the deployment of high capacity energy storage systems, to make up for their fluctuating rate of energy generation throughout the day. Li-ion batteries and Vanadium flow batteries have been used in large scale operations for this application. The soluble lead redox flow battery has been proposed as an attractive alternative in this field, due to the lower cost of installation and operation. However, widespread acceptance of the battery is hindered by poor cycle life, among other factors. Operation of the battery involves deposition and dissolution of solid deposits on the electrodes during charging and discharging, respectively. The lead dioxide deposit on the anode has been reported to have poor adhesion, and peel off from the substrate, leading to non-recoverable loss in efficiency for the ongoing cycle, and thereby reducing cycle life. In this work, an attempt has been made to study the impact that using a new carbon felt material consisting of interwoven fibres, as the electrode, can have on the adhesion. Galvanostatic experiments have been performed under conditions like earlier experiments with plane graphite electrodes. The new electrode shows promising performance in terms of cycle life, and efficiency, and an unusual feature in the decrease in energy efficiency with cycle numbers.

Measurement of glucose levels in human saliva using a disposable paper test strip

Shruti Soni, and Bhushan Toley

Diabetes Mellitus is a metabolic condition characterized by an increased level of glucose in the blood leading to hyperglycemia that can be due to insufficiency of the body to produce insulin (Type 1) or cellular resistance to insulin action (Type 2) or both. Diabetes can also be triggered during pregnancy and it risks the growth and development of the baby. Diabetes is difficult to cure but it can be managed by a healthy lifestyle, regular physical activity and proper monitoring of the glucose levels. The current method of diagnosis involves drawing blood samples and measuring blood glucose levels, by either sending blood samples to laboratories or using self-monitoring device at home. Patients suffering from diabetes are required to monitor their glucose level multiple times daily by drawing blood each time, which can be troublesome and can cause discomfort and trauma to the patients, especially children, older adults, and chronically ill patients. Therefore, there is a need for the development of non-invasive ways of monitoring diabetes. Whole saliva is mostly made of water (99.5 %) and other functional components such proteins, enzymes, electrolytes, mucus, antimicrobial agents and smaller organic molecules like glucose, lipids, nitrogen, urea, uric acid, etc. Saliva is known to change its composition and function when a person is suffering from the disease. Many studies suggest glucose level in blood and saliva are correlated1, although the level of glucose in the saliva is way less than that found in the blood. Saliva has the advantage of being one of the most abundant secretions in the human body. It involves a non-invasive way of sample collection and it can be easily stored without clotting, unlike blood.

We are developing a colorimetric paper-based device which can detect salivary glucose levels in the range 1 mg/dL to 30 mg/dL, which shows different color intensities depending upon the concentration of glucose present in the salivary sample. Using this device, we will be working with real human saliva in near future, and will be developing a correlation between blood and salivary glucose levels. In our study, we are targeting post-prandial glucose levels.

Modelling virological breakthrough due to resistance to antibodies during treatment interruption suggests avenues for prolonging HIV-1 remission

Ananya Saha and Narendra Dixit

Passive administration of broadly neutralizing antibodies (bNAbs) of HIV-1, like VRC01, targeting conserved regions of the HIV-1 envelope can prolong the viremic control achieved with antiretroviral therapy (ART) and provide long-term remission. However, treatments with bNAbs, especially when used singly, can fail due to resistance. In recent trials, VRC01 infusion to ART treated individuals during treatment interruption resulted in viral rebound despite the presence of sufficient VRC01 in circulation in most patients. We wanted to understand the dynamics of this breakthrough quantitatively to predict protocols that can maximally prolong remission. We developed deterministic and stochastic viral dynamics models under VRC01 therapy to describe recent clinical trials. HIV infection is invariably associated with the establishment of a latently infected cell reservoir. The absence of active viral replication during ART indicates the crucial role of latent cell reactivation in the observed breakthrough. Our model showed that the latent reservoir had to harbor pre-existing VRC01 resistant proviruses to achieve breakthrough within the clinically observed timeframes. We estimated the fitness of the resistant strains from an analysis of an independent in-vitro competition assay. Using the fitness values, we estimated an upper bound on the frequency of the pre-existent proviruses based on a mutation-selection balance. We then estimated the reactivation time of latent cells harboring resistant proviruses leading eventually to detectable viremia. Our estimates resembled clinically observed breakthrough times: ~4±2 weeks, observed in 12 patients in a recent trial. We then used our model to identify methods and/or protocols that would prolong remission. Our model predicts, for instance, that with the engineered bNAb VRC01LS, a VRC01 variant with 4-fold longer half-life than VRC01, the rebound time distribution can be significantly delayed to ~20 weeks with the same dosing protocol. Our study emphasizes the importance of quantitative modeling of passive bNAb therapy for maximizing remission times during ATIs.

Modelling flow through coronary arteries

Aadhil Basith A, and V Kumaran

Myocardial Fractional Flow Reserve (FFR) based on invasive coronary angiography, is the gold-standard for the assessment of the functional impact of a stenosis. The invasive angiography requires the placement of a pressure sensor guidewire near a stensois, which can lead to the overestimation of FFR. The purpose of this study is to predict a non-invasive analytical model of coronary FFR. The three-dimensional structure of the coronary arteries of a patient is obtained from the Computed Tomography scans using a software, 'Slicer 3D'. The centrelines of all the branches of the arteries are extracted using the software, 'Vascular Modelling Tool Kit', which automatically calculates the radius as a function of length of the arteriolar vessel. The proposed analytical model is derived from conservation of energy, which considers various energy losses along the length of a stenosis, such as energy loss due to sudden constriction and expansion as well as diffusive and convective energy losses. Accordingly, the total pressure drop across all the branches of the coronary arteries is calculated, which determines the FFR. The anticipated outcome of this model is to obtain the intensity of stenosis. FFR value of less than 0.80 indicates that the stenosis is severe.

Molecular dynamics of water molecules translocating through graphene nanopores

Sagar Bathla and K.G Ayappa

Porous graphene seems to have a great potential for membrane separation due to its atomic thickness and excellent transport properties and selectivity. Implementation of porous graphene with sub-nanometer pores as a 2D porous interface between contaminated water and air for low-energy water vaporization is a new concept. Molecular simulations have been employed to study the water dynamics through graphene nanopores. Two graphene pores namely pore-10 (10 carbon atoms are removed) and pore-16 (16 carbon atoms are removed) with pores terminated with hydrogen are considered with pore-size ranging from 3.13 Å to 4.69 Å for this study. Free energy computations were done to calculate the potential of mean force (PMF) or energy barrier faced by water molecule in translocating through the pores. It was found that a single water molecule faced a huge barrier of approximately of 25 Kcal/mol through pore-10 which is expected because of its small size of 3.13 Å. Through pore-16, relatively a low energy barrier of approximately 3.8 Kcal/mol is observed due to its larger pore size as compared to pore-10. These simulations performed by assuming the charges on the pore-edge atoms according to the OPLS/AA forcefield (C with q = -0.115 and H with q = +0.115) and charges on rest of the atoms on graphene surface are considered zero. Ab initio calculations are also performed to find the point charges on each atom on the porous graphene surface and PMF calculation is performed again to find the energy barrier with correct point charges on each atom. With new charges, PMF calculations for pore-16 has completed and nature of the plot for PMF around graphene pore-16 is found to be same but with different numerical values (5 kcal/mol). It was revealed that with increase in pore-size, energy barrier faced by water molecule in translocating through graphene nanopore decreases and effect of the charges of the graphene sheet on the PMF is significant.

Molecular dynamics of drug molecules translocating through efflux pump

Shivam Gupta and K.G Ayappa

Multi drug resistant bacteria have become a one of the most serious problem for the public health. Efflux pumps plays a major role in the export of the drugs out of the bacterial cells. The tripartite complex AcrAB-TolC is one of the major multidrug resistance transporter in Escherichia coli. AcrB is the inner membrane protein which combines with the membrane fusion protein AcrA and the outer membrane protein TolC. The homotrimer AcrB is the active part of the tripartite complex and it is responsible for the substrate binding and the energy transduction. Based on the available asymmetrical crystal structure of AcrB, the transport of the substrate by AcrB supports a functional rotating mechanism in which each monomer of AcrB supposed to be in different states[Access(A),Binding(B),Extrusion(E)].Here we explored the molecular level description of the conformational changes during the functional rotation mechanism and their relationship with the substrate extrusion by using molecular dynamics simulation. By using the protonation states for the titratable residue Asp408, our simulations revealed the relation between the side chain configuration and the specific protonation state. It was found that the alteration of the protonation state in the transmembrane domain induces the functional rotational mechanism in the porter domain which is primarily responsible for the substrate extrusion.

Heterogeneity in arabinose operon gene expression in bacteria

Ratnasri K[1], *Rohit Dutta*[2], *Chetana Baliga*[2], *Raghavan Varadarajan*[2] *and Rahul Roy*[1,2,3]

[1]*Centre for Bio Systems Science and Engineering,* [2]*Molecular Biophysics Unit,* [3]*Dept. of Chemical Engineering, Indian Institute of Science, Bangalore*

The ability to conditionally control the expression of specific genes using external inducers is useful to study the effect of gene products on cell physiology. Inducible plasmid systems are designed for a variety of applications, ranging from gene over expression for protein purification to low basal level expression for studying toxic gene products. Hence, a highly controlled system which provides linear gene expression output is desirable.

The arabinose inducible pBAD series of bacterial vectors offer such a tuneable and tightly regulated system for gene expression. At the population level, expression from this promoter is graded, with medium levels of expression at intermediate levels of arabinose. However, studies have shown that the arabinose expression vectors have an all-or-none response at the single cell level. Initially attributed to the heterogeneity in the expression of the transporter AraE, this phenomenon persists in non-arabinose metabolizing cells even with a constitutively expressed transporter.

High gene expression noise, which is a measure of cellular heterogeneity, is particularly pronounced in promoters under low inducer levels. In addition to intrinsically present stochasticity, this noise might further be amplified by the architecture of the gene network motifs. Previously, we reported a bimodal distribution of fast degrading version of (fd)GFP expression cloned under the PBAD promoter at intermediate inducer levels. Interestingly, bulk level mRNA quantification showed similar transcript levels between GFP-positive and GFP-negative cells, possibly indicating post transcriptional regulation of gene expression in the cells.

Combined with fdGFP expression monitoring, that captures protein dynamics more efficiently than its long lived wild-type counterpart, we employed a single molecule RNA quantification technique, smRNA-FISH, to determine whether the observed protein heterogeneity indeed stems from transcriptional heterogeneity at the single cell level. In this technique, GFP mRNA are labelled with multiple Cy5 tagged probes.

Fluorescence microscopy and subsequent processing of the micrographs is done to determine the RNA count per cell. Simultaneous single cell GFP imaging is also done to capture protein level heterogeneity. Such co-analysis of transcription and translation can provide insights into the origin of heterogeneous gene expression.

Rheology of cohesive granular powders

Peter V. Dsouza, Rahul A. Kumar and P R. Nott

Several industrially useful powders are cohesive and do not flow freely making transport and handling difficult. These powders are cohesive due to either van der Waals forces or the presence of liquid bridges between them. Despite their importance, it has proved a challenge to characterise the flow behaviour of these powders. The rotary drum is traditionally used to test for the flow properties of cohesive granular particles wherein they undergo avalanching motion. Dry powders, in comparison, are free flowing and do not form avalanches. This avalanching frequency has thus been a measure of cohesion.

In this work, we test a series of food particle mixtures by shearing them in a rotary drum. We capture avalanching behaviour of the powders using high speed imaging. We correlate the variation of the avalanche height with space and time to characterise to size and life of the avalanches formed. Comparing these correlations between samples gives us a rudimentary measure of particle cohesion that is still more detailed than avalanche frequency.

Molecular Modeling of Gas Hydrates

Shivanand Kumar Veesam and S Punnathanam

Clathrate hydrates are nonstoichiometric crystalline inclusion compounds in which the host lattice is made up of water molecules that are tetrahedrally bonded to each other via hydrogen bonds and guest molecules consist of typically small gas molecules, such as methane, ethane etc.1 The crystalline structure of the host lattice contain cavity like structures, which are occupied by the guest molecules. Traditionally, thermodynamics of gas hydrates is described by van der Waals and Platteeuw (vdWP) theory2 which models the clathrate hydrate as an adsorbent and the cavities as adsorption sites. In this theory,2 the host lattice is assumed to be rigid; each cavity can contain at most one guest molecule; guest-water interaction is limited to the nearest neighbor water molecules forming the cavity; and guest molecules do not interact with each other. The guest-water potential parameters and empty hydrate properties are usually regressed from experimental phase equilibrium data.1 Chialvo et al. suggested that the success of the vdWP theory is due to presence of large number of adjustable parameters used in the regression of equilibrium data and the theory acts as a data correlator. There has been a lot of work over the years to overcome these shortcomings of the original vdWP theory. Several studies showed that guest-water interactions beyond the first cage are significant enough to influence the phase equilibrium predictions. Other studies have pointed out that guest-guest interactions are also significant to influence the phase equilibrium predictions. In this context, Punnathanam and co-workers3,4 showed that the rigid host lattice approximation is a significant source of error while predicting the phase equilibrium. To overcome this drawback, Ravipati and Punnathanam5,6 developed a method to compute the contribution of movement of water molecules in the host lattice to the partition function of the clathrate hydrate. The work of Ravipati and Punnathanam6 successfully demonstrated the accuracy of the modified vdWP theory using the phase equilibrium data computed using molecular simulations. In this work, we apply the modified vdWP theory to model the experimental phase equilibrium data, and recompute the guest-water potentials. The empty hydrate reference properties are

directly computed from molecular simulations. The modified vdWP theory allows us to substantially reduce the number of regressed parameters to two per guest molecule while achieving accuracies comparable to those predicted by CSMGem1 program which contains 13 regression parameters. In addition, our method can also predict the hydrate cage occupancy accurately.

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Single particle tracking to probe membrane protein/peptide interactions

Satyaghosh Maurya and Rahul Roy

Single molecule methods like single particle tracking, super-resolution microscopy, and foster resonance energy transfer have gained prominence recently in the field of membrane protein/peptide dynamics. These methods have the advantage as they allow us to investigate single molecules individually and in real time, unlike crystallography or electron microscopy.

The two cases where we have applied some of these methods are 1) to understand the assembly mechanism of pore-forming toxin Cytolysin A (ClyA), 2) and the mechanism of membrane disruption by anti-microbial peptides (AMPs).

Here, we use single particle fluorescence microscopy to examine the events in the pore formation pathway of ClyA on supported bilayer membranes. We demonstrate how cholesterol is a critical component for effective pore formation and a possible means for selective targeting by PFTs. Binding of ClyA, on supported lipid bilayers, was rapid and complete within seconds. From diffusional and trajectory analysis of single ClyA proteins, we observed that the protein transitions between a high and low mobility state via an intermediate. We argue that the lowest mobility state represents a stable membrane-bound protomer along the assembly pathway. This 'immobilization' kinetic is accentuated in bilayers with cholesterol highlighting its role in ClyA pore formation. Furthermore, fluorophore photobleaching analysis of the ClyA oligomers at physiological concentrations suggested that cholesterol enhances the fraction of oligomers leading to pore formation possibly by stabilizing the assembly intermediates mainly protomer-protomer interactions. This dual role of cholesterol at two distinct steps in the pore-formation pathway of ClyA can explain the molecular mechanism giving rise to high selectively in targeting mammalian cells. Additionally, mutational studies in the regions which are interacting with the cholesterol as suggested by molecular dynamics simulations offer more evidence of ClyA's interaction with the lipid bilayer. Together with Single molecule experiments and molecular dynamics simulations, we have tried to unravel the molecular

mechanisms through which CytolysinA affects and selectively target the mammalian cells.

Anti-bacterial peptides bind and disrupt the bacterial membrane, often leading to cell death. They can also lead to more subtle manipulation of the cellular functions. We use single particle tracking on supported bilayers to understand the behaviour of these peptides interacting with the membrane to decipher the possible ways these AMPs disrupt the bacterial membrane.

Dengue virus diversity revealed by clinical metagenomics

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Dengue virus (DENV) is a mosquito-borne Flavivirus with a single-stranded RNA genome that causes an estimated 390 million infections worldwide every year. In India there are four closely related serotypes of DENV (DENV-1 to DENV-4) co-circulating simultaneously. It has been known that monotypic infection is generally asymptomatic, but heterotypic dengue infection is associated with severe dengue. Similarly, intrahost diversity of virus allows it to adapt to selection pressures and escape the immune response. Understanding their genomic diversity and evolution during infection is crucial to develop better vaccines.

To probe the viral diversity during infection, we sequenced viral RNA from 223 dengue infected patients from three major hospitals across the country. We recovered 96 whole genome sequences with >5X coverage and additional 11 genomes with >1X coverage. Multiple sequence alignment followed by phylogenetic analysis showed that almost all sequences clustered close to known Indian strains.

The inter and intrahost variant analysis of the two dominant serotypes (DENV-1 and DENV-2) shows the mutation hotspots and coldspots in the dengue genome. The conserved antigenic regions across the genome can be used as potential targets for developing the vaccine.

Simulating the effect of flow and trajectory dynamics on metastatic ovarian cancer cells and their multicellular collectives

Sreepadmanabh M, Kavyashree Rai and Bhushan Toley

Cancer cells show novel behaviors by exchanging chemical and mechanical cues with their surrounding microenvironment. Ovarian cancer metastasizes within a highly dynamic fluid milieu of the peritoneal cavity, wherein shear stresses due to the flow of the accumulated fluid (ascites) can exert significant influence over tumor progression. Understanding the precise nature of this interaction, and characterizing the regulatory mechanisms involved could provide valuable insights towards the design of effective therapeutic strategies. To this end, we have designed a microfluidic setup to simulate the effects of fluid dynamics on metastatic ovarian cancer cells and their multicellular aggregates called spheroids. Using this setup, we show that the spheroidal organization confers broad survival advantages to metastatic cells in a suspended flow environment, although the latter leads to morphologically smaller and rounder spheroids. This could allow for a significantly enhanced capability to successfully migrate and establish secondary tumors – a hypothesis that is motivated by our preliminary findings based on cell viability studies. We further proceed to demonstrate that variations in both the direction and duration of flow impairs the survivability of cancer cells. Furthermore, we have attempted to model the nature of flow within our microfluidic setup using COMSOL-based particle tracking modules. We hope to extend and expand on this study by analyzing metastasis-specific molecular markers, optimizing more comprehensive cell-viability assays, assessing the potential contributions of flow-induced phenotypic changes towards chemoresistance, as well as developing robust models of spheroid genesis and spheroidal disaggregation under suspended flow.

A large-volume sputum collection and dry-storage device for tuberculosis molecular diagnostic testing

Andrea Dsouza, Saylee Jangam, and Bhushan Toley

We report a device for the collection and dry stabilization of sputum samples for storage and downstream molecular diagnosis of tuberculosis. Till date, devices for dry storage of sputum have not existed – this is the first device of its kind. Current specimen stabilization methods have largely relied on the dry blood spot (DBS) technology, which i) can only collect very small specimen volumes, ii) increases the risk of exposure by having to dry the DBS in open air, and iii) increases the risk of cross contamination during analysis because of the need to punch paper disks from DBSs. In addition, such stabilization methods have not been optimized for other specimens like sputum, urine, etc. We have developed a specimen transportation device (SPECTRA-tube) that can spread a large specimen volume (> 1 ml) over a paper membrane and dry the specimen rapidly within an enclosed device. The dried sample can be entirely recovered by rehydration and centrifugation, obviating the need for punching. Different membranes were tested for their efficiency of sample recovery using centrifugation; Standard 17 glass fiber was found to be most efficient at releasing dried reagents. SPECTRA-tube, therefore, consists of a stack of two 8 cm x 2 cm layers of Standard 17. A 1.2-ml 3x diluted mock sputum (viscosity 350 cP) solution introduced into SPECTRA-tube dried in < 8 hours. Moreover, the compatibility of SPECTRA-tube with downstream molecular testing was assessed by spiking Mycobacterium smegmatis (MSM) into 3x-diluted mock sputum and storing 1.2 ml of this solution in the SPECTRA-tube. Stored sputum was recovered on days 1, 3, and 5 and the concentration of MSM was detected by qPCR following DNA extraction, showing that MSM bacteria were detectable even after 5 days of storage. This is the first report of a device that can dry and stabilize sputum for downstream molecular testing. This represents a significant advance in specimen storage technology and overcomes all limitations of DBS cards enlisted above. While demonstrated for sputum here, this is a platform technology that can be used for dry stabilization of large volumes of any liquid specimen.

Attenuation of HIV replication fitness among men who have sex with men (MSM)

Ananthu James and Narendra Dixit

Depending on how HIV is transmitted, populations are classified into three main categories: men who have sex with men (MSM), heterosexuals, and injection drug users (IDU). They are characterized by disproportionate prevalence of different HIV subtypes and the presence of transmission clusters (multiple transmissions among the same category, without involving the rest), indicating low levels of mixing between them. This suggests the possibility of viral strains being specifically adapted for each transmission category. Each transmission event results in reduction of the viral replication fitness (number of secondary infections from an already infected host cell) due to accumulation of resistance mutations to oppose host immune system, consequently leading to adaptation. Based on the data from large populations from China and Europe, we show that MSM specific strains are the most adapted ones among all the transmission category specific viral strains, and hence have the lowest fitness. This could be because the probability associated with transmissions among MSM being much higher relative to other categories, along with their increased association with transmission clusters. We discuss the possible causes and consequences of these findings.

Visual detection of SNP using molecular beacon for detection of first line drug resistant tuberculosis

Ketan A.Ganar and Bhushan Toley

Mycobacterium Tuberculosis is the causative agent for Tuberculosis (TB), one of the oldest diseases leading to high mortality rates. The global TB report 2018 states 10 million cases of Tuberculosis, India sharing 27% of the global TB burden. Although the development of antibiotics has helped in disease management, but inappropriate usage of antibiotics has led to the evolution of bacteria to multiple drug resistant Mycobacterium Tuberculosis species (MDR-TB). One of the mechanisms by which Mycobacterium Tuberculosis develops resistance is by incorporating mutations in the bacterial gene. Failure of first line drug, rifampicin (RIF) in MDR-TB is due to mutations in the 81bp rifampicin resistance determining region (RRDR) of the RNA polymerase beta subunit (rpoB). The nature of amino acids at position 526 and 531 are majorly associated with RIF resistance. The change in amino acid at 526th position from histidine (CAC) to tyrosine (TAC) signifies the presence of MDR-TB species. Early and timely detection of these mutations can determine the nature of pathogen (sensitive/resistant) hence facilitating appropriate therapeutics. Molecular beacons are single stranded DNA molecules, widely used to differentiate single nucleotide polymorphism (SNP). In current study, we have developed a fluorescence-based assay to visually differentiate single nucleotide polymorphism associated with drug resistance in Mycobacterium Tuberculosis.

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