

Developing antimicrobial biomacromolecules

SCELSE and the School of Chemical and Biomedical Engineering have been recently awarded a 5-year \$10m grant from the Ministry of Education to develop novel selective cationic antimicrobial biomacromolecules (CAMBs) as next-generation antimicrobial agents. The research team which is led by PI Prof. Chan Bee Eng (Mary Chan-Park) includes A/Prof. Liu Xuwei and Thomas Dick (NUS), and Nanyang Asst. Prof. Kimberly Kline (SCELSE) and Duan Hongwei.

SCELSE is providing a technological and scientific platform for several aspects of the project, especially to understand the interactions with pathogens and the mechanisms of action of the novel biomacromolecules. The Centre's capacity to undertake in-depth analyses of microbial communities



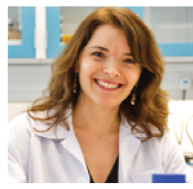
Prof. Mary Chan-Park

in any system, is supported by well-established expertise in high-resolution meta-'omics, systems biology, biofilm mechanism and engineering platforms.

Specifically, identifying the mechanisms of action of these new antimicrobial materials requires high throughput 'omics technologies at various levels including whole cell/ systems. This includes DNA sequencing to identify mutants that may develop resistance to the biomacromolecules and RNA sequencing to highlight the genes responsible for resistance. Metatranscriptomic analyses of bacteria exposed to the biomacromolecules developed in the project will also identify ways in which they respond to environmental conditions.

"The cationic polysaccharide molecules that Mary Chan's group has

discovered are extremely interesting because they are very potent in killing bacteria but we have no idea how they are working. We're very excited to help her figure out their mechanism of action as part of this Tier 3," Asst. Prof. Kim Kline said.



Asst. Prof. Kimberly Kline

The investigation is based on the elegant idea of combining in a single co-polymer molecule two different functions: preferential selection of microbe cell walls over mammalian cell surfaces, and microbe membrane disruption capability (Li et al., 2011 & Dong et al., 2012). Their initial designed compounds, cationic chitosan-based graft co-polymers, have displayed a unique combination of both ultralow toxicity and efficient broad spectrum antimicrobial activity. These cationic chitosan derivatives contain a polysaccharide (PSa) backbone, (a derivative from

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Calendar

SCELSE Seminars
11am -12pm, SBS-08

22 May: RIP, Li, Cheng & Nandini, Shome.

Jun-05: Prof. Atul Parikh, NTU

Jun-12: Prof. Stefan Wuertz

Meetings

Environmental Engineering meeting:
Fridays 9am, B3 Meeting Room

Programs

Aug '14 & Jan '15: Biophysical Platform Program, open for student intake. <http://www.scelse.sg/programs>

Conferences 2014

24-29 August: 15th International Symposium on Microbial Ecology. Seoul, S. Korea.

5-6 Sep: Academic Medicine – Transforming Vision into Reality: SingHealth Duke-NUS Scientific Congress 2014, Singapore General Hospital.

10-12 Sep: The Perfect Slime - Nature, Properties, Regulation and Dynamics of EPS, IWA Conference, Essen, Germany.

NTU and Nature Publishing Group collaborate through SCELSE

SCELSE's initiative to establish a *Biofilms and Microbiomes* journal has been realised with the collaborative efforts of Nature Publishing Journal (NPJ) and Nanyang Technological University.

"The first publication issue will be launched in Vienna in early 2015," Prof. Yehuda Cohen said, who helped coordinate the journal's establishment.

Aimed to be a high impact journal, it will cover topics from nasal and skin microbiomes to industrial, health and environmentally relevant biofilms.

SCELSE- SAB member Prof. Staffan Normark from the Karolinska Institute and former organizer of the Nobel Laureate Conference (Sweden) will be the editor in chief of the journal.



Prof. Staffan Normark

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Biophysics of Biofilms Workshop Tools, applications and dimensions

SCELSE recently hosted its first Biophysics of Biofilms workshop. Lecture presenters included Prof. Yehuda Cohen, A/Prof. Sanjay Swarup, research fellows Dr Karinh Eurenus and Dr Tom Seviour, PhD student Chew Su Chuen, and research assistants Myat Thiri and Vishal Prajapati. The aim of the workshop was to provide a better understanding on life at microscales, current biophysical tools for biofilm characterization, applications available to elucidate biofilm settlement development and dispersal, and the function of biofilm architecture. Different topics were addressed in the lectures, from biophysical characterization platforms to biofilm matrix dynamics, composition and diffusivity, to microfluidics and electroconductivity, as well as first insights to biofilm growth chambers to mapping metabolomics.

Saravanan Perisiamy Research Fellow

The perks of coupling up can be easily identified in microbial communities. Saravanan's current research focuses on dual species biofilm models and understanding how species coupling benefits biofilm dynamics. Specifically, his work on biofilm metabolomics focuses on mapping metabolic pathways in mono and mixed species biofilms. His greatest challenge is to study small distinct molecules by targeted and untargeted global approaches. One of Saravanan's major projects, "Biofilm competition and coexistence – a dual species biofilm model", uses a chambered microscope slide (static system) and flow cells to study the pair-wise combinations of *Pseudomonas aeruginosa* PAO1, *Pseudomonas protegens* Pf-5 and *Klebsiella pneumoniae* KP-1 when grown as biofilms. He is describing the roles of *P. aeruginosa* PAO1

exopolysaccharides in mixed species biofilms, as well as detecting and assigning function to "intra-cellular and extra-cellular metabolites".



Saravanan working with dual species biofilms.

"SCELSE is the best environment to collaborate", he says, as he works with a number of experts across different disciplines inside and outside the centre. He has been involved in a number of student projects in SCELSE, and is currently collaborating with Prof.

Sanjay Swarup and senior research fellow Victor Nesati (SCELSE-NUS Environmental Research Institute (NERI)), and research fellow Desi Stuti (Mechano-biology Institute, NUS) in a project involving the role of SsrA and SsrB in *Salmonella enterica* biofilm formation. Saravanan has

also been co-supervising PhD student Tanujaa Suriyanarayanan from Prof. Sanjay Swarup's lab (NUS) on her project titled "The impact of flagellin phosphorylation in *Pseudomonas aeruginosa* biofilm development and secretome". They are studying the mechanism of multispecies biofilms and how these species' communities are protected in stressed environments.

Saravanan obtained his BSc in 1998, and his MSc in 2000 at the Ayya Nadar Janaki Ammal College, Sivakasi, which is an affiliate of the Madurai Kamaraj University of India. In 2006, he completed his PhD in Biotechnology at Pondicherry University, (India). For his doctoral dissertation titled "Ecological and molecular identification of bacteria isolated from condenser discharged site of a coastal electric power plant," he characterised exopolymeric substances (EPS) produced by biofilm forming marine bacteria.

Saravanan loves playing tennis, as well as badminton and swimming.

Publication profile

To address the links between quorum sensing (QS), organisation and composition of complex microbial communities, SCELSE researchers performed a long-term bioreactor ecology study. They observed that the conversion of floccular biomass to highly structured granules was interestingly correlated to *N*-acyl-homoserine-lactone (AHL)-mediated QS. Species-rich communities in natural habitats are usually found within a matrix or extracellular polymeric substance (EPS), either as surface

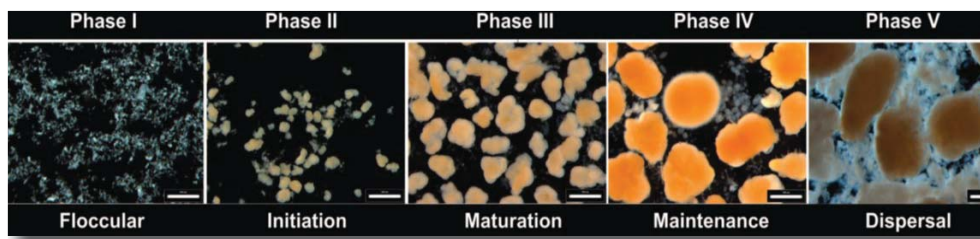
Life in granular communities

SCELSE researchers found homoserine-lactone-mediated quorum sensing in microbial communities organised as granules.

associated biofilms or surface independent floccular aggregates. Formation and dispersal of these biofilms results from environmental changes, including nutrient concentrations, oxygen,

temperature etc. These organisation dynamics may be a common feature in many natural and engineered ecosystems. This study is significant because metadata analysis showed

how changes in EPS relate to granulation processes, and that AHL mediated QS seems to be a key factor within granular or structured floccular communities.



Particle size distribution (measured on a volume basis) and sludge volumetric index (SVI₁), of a granular sludge community in a sequencing batch reactor based on microscopic visualisation of structures.

The ISME Journal (2014), 1–12
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www.nature.com/ismej

ORIGINAL ARTICLE

The role of quorum sensing signalling in EPS production and the assembly of a sludge community into aerobic granules

Chuan Hao Tan^{1,2,3}, Kai Shyang Koh¹, Chao Xie¹, Martin Tay^{1,2,4}, Yan Zhou², Rohan Williams¹, Wun Jern Ng^{2,3}, Scott A Rice^{1,4,5} and Staffan Kjelleberg^{1,4,5}

Experimental Design and Data Analysis Workshop

SCELSE
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Dr Ezequiel (Ziggy) Marzinelli gave a workshop to SCELSE students on experimental design and data analysis from real ecological and environmental studies. During April, students benefited from lectures to practical exercises/case studies on biological problems, and on tools available for efficient data analysis and interpretation.

HSH Prince Alfred of Liechtenstein visits SCELSE



HSH Prince Alfred of Liechtenstein (left), Chairman of the International Peace Foundation (IPF) in Vienna, recently visited SCELSE. During his visit, Prof. Yehuda Cohen presented (above) SCELSE's biofilm research and discussed the launch of NTU-Nature partner journal "Biofilms and Microbiomes" in Vienna.

From right to left, Professors Stefan Wuetz and Yehuda Cohen welcomed HSH Prince Alfred and Mr Uwe Morawetz (founder of IPF) to SCELSE.

Genome Biology and Evolution

gbe.oxfordjournals.org

Genome Biol Evol (2014) doi: 10.1093/gbe/evu094
First published online: May 6, 2014

Comparative genomic analysis of malaria mosquito vector associated novel pathogen *Elizabethkingia anophelis*

Jeanette Teo^{1,1}, Sean Yang-Yi Tan^{2,3,1}, Yang Liu², Martin Tay^{2,3}, Yichen Ding², Yingying Li³, Staffan Kjelleberg^{2,4}, Michael Givskov^{2,5}, Raymond T.P. Lin¹ and Liang Yang^{2,3,*}

Latest SCELSE
publications

small

Reactive Oxygen Species

Rhodamine-Modified Upconversion Nanophosphors for Ratiometric Detection of Hypochlorous Acid in Aqueous Solution and Living Cells

Yi Zhou, Wenbo Pei, Chenyuan Wang, Jixin Zhu, Jiasheng Wu, Qinyu Yan, Ling Huang, Wei Huang, Cheng Yao, Joachim Say Chye Loo,* and Qichun Zhang*

small 2014,
DOI: 10.1002/sml.201303127

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Developing Antimicrobial Biomacromolecules (from p. 1)

microbicidal polymers and peptides). Non-polysaccharide based polymers and peptides which have an efficient antimicrobial activity, do not exhibit such low mammalian cell toxicity. The similarity of the agents' polysaccharide content with the polysaccharide-rich cell walls of bacteria enhances diffusion and microbial selectivity. Cell walls of bacteria are rich in polysaccharide, peptidoglycan (PG) or lipopolysaccharide (LPS), and both are native polysaccharide-based co-polymers. In contrast, mammalian cells do not have the polysaccharide-based PG/LPS-containing cell wall layer. The combination of microbe cell wall mimicry and a developed cationic polysaccharide-peptide co-polymer is a completely new approach in CAMBs research.

The overall objective of this programme is to develop cationic

antimicrobial polysaccharide-peptide co-polymers with high bacterial killing efficacy and reduced toxicity for diverse applications, through studies on associated composition design principles and mechanisms for selective bacterial killing.

New antimicrobial agents are in growing demand in a number of fields, ranging from medicine to personal care and agriculture. This is significant because current antibiotics are becoming increasingly ineffective towards "superbugs" such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecalis* (VRE) and other resistant forms of some life-threatening infections such as pneumonia, tuberculosis, meningitis and endocarditis. Far from the medical standpoint, there

is a need for increasing regulatory pressures for higher safety standards and more potent agents (germicides and disinfectants). This is important for diverse applications, including sanitation in healthcare settings, drinking water purification, food processing and personal care products. There is an urgent need for alternative potent but safe antimicrobial agents that will not develop microbial resistance.

References

Li, Peng, et al. "A polycationic antimicrobial and biocompatible hydrogel with microbe membrane suctioning ability." *Nature Materials* 10.2 (2011): 149-156.

Dong, Xiao-Chen, et al. "3D graphene-cobalt oxide electrode for high-performance supercapacitor and enzymeless glucose detection." *ACS nano* 6.4 (2012): 3206-3213.

Biophysical Platform Program

SCELSE is offering a multidisciplinary and holistic Biophysical Platform program with research projects focusing on both fundamental and applied science. The project covers diverse fields, stretching from mathematics, physics, biology and chemistry to materials science, life science engineering and biophysics.

"We want to use this multidisciplinary and holistic view in the Biophysical Platform Program in order to find new candidate materials for sustainable energy devices," SCELSE senior research fellow Dr Karinh Eurenus said.

Biofilms are both adhesive and fast growing as well as cheap in production costs and offer a vast variety of possible species combinations. Nano-engineering multispecies biofilms (NEMSBS) offer a strong structure and increased conduction, which are two important components for energy devices such as fuel cells, batteries and transistors.

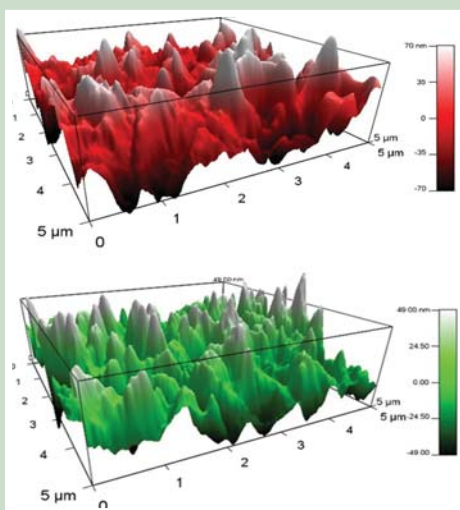
The aim of the program is to analyse fundamental structural properties of NEMSBS and how they affect conduction, thereby determining if they are suitable candidates for sustainable energy devices.

PhD projects are directed towards NEMSBS for use in sustainable energy devices, as electives for IGS students of the August 2014 and January 2015 intake.

For more information, please contact Dr Karinh Eurenus (karinh.eurenus@ntu.edu.sg)



Dr Karinh Eurenus



Atomic Force Microscopy (AFM) images capturing the topographic features of *Pseudomonas aeruginosa* wildtype (PA01, red) and its over-produced amyloid mutant (+FAP, green) biofilms, grown on conventional and mica glasses, respectively.

NTU and NPG through SCELSE (from p. 1)

"NTU's partnership with NPG to establish a new open access Nature Partner Journal (NPG) *Biofilms and Microbiomes* is timely, as the university ramps up formation of a new Life Science and Biomedical research cluster," said NTU President Professor Bertil Andersson (picture below).

"This new publication platform will bring together scientists studying the social behaviour of complex microbial communities across a wide disciplinary spectrum and covering natural, medical and industrial settings," Bertil continued.

"NTU is always looking for such opportunities to play our part in pushing the frontiers of new, emerging fields," he said.

The soft launch of the journal *Biofilms and Microbiomes* took place at the Biofilms 6 conference in Vienna, Austria.



From right to left standing, Ms Rebekah Yang Jia Yue (Tsukuba University, Japan and alumni of SCELSE's summer course 2013), and SCELSE PhD students Mr Ng Chun Kiat, Mr Kelvin Lee, and Mr Kumaravel Kandaswamy, behind SCELSE deputy director Prof. Yehuda Cohen, who is sitting next to NTU President Prof. Bertil Andersson, Prof. Patricia Conway (UNSW) and SAB member Prof. Staffan Normak at the Biofilms 6 conference in Vienna, Austria.

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