



APPEL À PROJETS RECHERCHE PARIS-NUS 2021 : PROJETS PROPOSÉS AU FINANCEMENT

FACULTÉ DE SANTÉ

Automated machine learning detection of craniofacial and ocular congenital abnormalities on simple face photographs

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Clinical detection of malformative conditions affecting the face/eyelids/eyes in children can be subtle, raising difficult diagnostic challenges. Their early detection is however important because they can herald more severe ocular or cerebral dysfunction like glaucoma, retinopathies, or associated cerebral conditions. More than a third of rare genetic conditions are associated with facial characteristics. Their detection is mandatory, leading to subsequent confirmatory genetic testing, which is expensive and not easily available. This first step of clinical detection depends largely on the personal experience of the examiner, which is however highly variable. Analysis of facial pictures may represent an interesting alternative, but is still subjective and dependent on human experience. Based on our previous experience in Ophthalmology, published recently in *The New England Journal of Medicine*, we propose to create a similar artificial intelligence based deep learning system able to identify automatically facial/eyelids/ocular malformations that can lead to detection of underlying, often treatable genetic conditions that can affect the health of the eyes/brain.

For this purpose, we propose to combine two unique expertises: (1) facial dysmorphology in Paris, France (Necker – Enfants Malades University Hospital, one of the leading centres for rare diseases worldwide which will provide a very large collection of photographs and associated reference diagnosis) and (2) AI-based methods in ophthalmology and medicine at the National University of Singapore, an internationally recognized leader of this approach. Our project is to build a diagnostic tool using AI- based methods focused on the face and more particularly on the eye and eyelid region.

The pictures will be used to develop dedicated algorithms according the state-of-the-art deep learning methods, in order to predict the presence of craniofacial malformations based on eye and eyelid characteristics.



A subgroup of 50 conditions will be considered and the database on which we will work will include a total of over 400,000 pictures. Furthermore, the eyes may include numerous little-known morphological clues that are difficult to assess using standard diagnostic methods, such as subtle colour variations of the iris and moderate shape modifications of the eyelids. AI-based methods will identify the presence of this hidden data, that will be secondarily analysed and provide insight on potentially clinically relevant aspects of the developmental processes leading to eye and eyelid development.

In brief, our project consists in combining the skills of two highly competitive teams from Paris and Singapore in order to answer a scientific question leading to 1/ straightforward clinical applications (diagnostic tools for malformative diseases – that can be associated with ophthalmic and cerebral conditions) and 2/ insights into fundamental questions of developmental biology. This unique alliance is only a first step and it should subsequently lead to further larger scale funding for in depth project in both countries.

Understanding islet cell interactions to facilitate precision medicine in diabetes

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Type 2 diabetes (T2D) is a debilitating chronic disease that has spiralled out of control, affecting more than 400 million individuals. In the Western population, obesity and insulin resistance contribute to eventual pancreatic beta cell exhaustion and apoptosis. In Asia where more than 60 % of all diabetes cases occur, inferior pancreatic beta cell mass and/or function has now been clearly established as the underlying cause of diabetes. Here, we hypothesise that diminishing beta cell number and function allow the other islet cell types such as alpha cells and delta cells to predominate in an unchecked manner, resulting in uncontrolled hyperglycaemia. This is a new hypothesis that decreases the beta-centric view of T2D, by highlighting new cell targets. We propose to study islet cell interactions in physiological and pathological conditions so as to be able to modulate the balance in hormone secretion that determines glucose homeostasis. Rodent islet cell interactions will be studied in great detail in Dr. Scharfmann's lab in Paris. Human stem cell-derived beta and alpha cells will be studied in detail in Dr. Teo's lab in NUS. These rodent and human islet cells will be challenged with diabetes-relevant inflammatory stressors to evaluate their interactions under pathological diabetes conditions. Findings between Dr. Scharfmann and Dr. Teo's labs will be compared to identify similarities and differences (if any) in these cellular interactions that are not well understood to date. The changes occurring to and in these islet cell interactions from physiological to pathological states will be of significance as they will reveal mechanisms underlying dysregulation of glucose homeostasis. Overall, we posit that this study on islet cell interactions is of immense importance given that beta cells are purportedly more prone to stress, apoptosis and dysfunction as compared to the other islet cell types, this idea being supported by a limited amount of data. A thorough understanding of how these islet cell types interact and antagonise the function of each other will be key to facilitate efforts in applying precision medicine for our T2D patients.



FACULTÉ DES SCIENCES

Understanding the Dynamics of Flexible Sheets in Viscous Flows

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Fabricating flexible 2D materials such as graphene and polymer sheets via liquid-phase processing involves their motion and deformation in viscous liquids that considerably influence the material property and morphology of the fabricated sheets. Moreover, flexible sheets have been adopted as soft propulsors and actuators in biomimetics and micro-systems, whose performance critically depends on the interaction between the deforming sheets and flowing liquids. Here, we propose a combined experimental and numerical study to attain a fundamental understanding of how a thin flexible sheet behaves in viscous fluids. The motion of a deforming sheet in canonical flows and its dependence on the rest shape and flexibility of the sheet will be investigated, allowing us to potentially explore a flow-based strategy to control the sheet morphology. The propulsion of a sheet actuated indifferent means will be also studied, with an aim to identify the optimal strategy maximizing the thrust. The outcome of the project will provide helpful information to facilitate the fabrication of electronic or polymeric 2D materials and the design of sheet-like soft devices. Uniting their respective expertise in experiments and simulations, this project will synergize the Parisian and NUS research teams that are naturally complementary, paving the way for their long-term collaboration and endeavour in the broader area of fluid-structure-interaction and soft matter physics.

Actin superstars: mechanical impact in tissue organization and homeostasis

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Remodelling events in epithelia are accompanied by active cellular machinery that serves to constantly ensure connectivity and transmission of essential information between cells. Along this line, the actin cytoskeleton has emerged as an important player for regulating epithelial morphogenesis, and its functions in this context are wide-ranging. Recently, by using intestinal organoids as a working model, the Paris team discovered a unique multicellular actin assembly specifically located in the basal domain of the columnar differentiated epithelium. This cytoskeletal network constitutes a large-scale inter-connecting meshwork in the differentiated cell compartment. Interestingly, it has not yet been described in mammals, and its structural and functional characterization is still lacking. Based on our preliminary data, we hypothesize that such structure may play an instrumental role in coordinating the dynamic stress distribution across multiple cells and tissues. Additionally, it may serve to provide distinct but complementary mechanical constraints at the epithelial cell center and as well as at cell-cell interfaces.



We propose that the actin star network may function as a self-organized long-range mechanical communication apparatus which orchestrates the maintenance of cell shape, density and scaling, as well as the restriction of collective cell movements. To address our hypothesis requires the use of a full repertoire of micro-mechanical tools that precisely control physical parameter of the cellular environment, take measurement of the forces exerted within epithelia, as well as provide high-resolution imaging capability. These tools must then be integrated to state-of-the-art live cell microscopy and gene expression modulation. The Paris and NUS assembled teams provide the required depth of expertise for all aspects of the project. Understanding the organization and the molecular composition of the actin star network, its roles at the level of the differentiated epithelial compartment and the whole organoid expansion, and its coupling to mechanical signals due to various external conditions that include tissue stiffness or geometry, could have important implications in physiological and pathological conditions such as epithelial homeostasis and cancer progression.

FACULTÉ SOCIÉTÉS ET HUMANITÉS

Political economy of China's Outward Foreign Direct Investment in Southeast Asia: An Assessment

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The proposed research will analyze the determinants of China's Outward Foreign Direct Investment (OFDI) in Southeast Asia and potential impact on bilateral relations economically and politically. China's OFDI in Southeast Asia is one of the most important development in bilateral economic ties in the last two decades. Following its "Going Global" policy announced in 1999, China's OFDI in the world has grown rapidly, especially in the past decade when China actively pursued its Belt and Road initiative. The rapid growth of China's OFDI in the region signifies a potential reshuffle in economic and political relations between China and Southeast Asia. As such, it is imperative to investigate China's motivations for OFDI and assess potential impact so that the region can be better prepared for the future.

The analytical framework for the research is based on Regulation Theory. The hypotheses of Regulation Theory will help us to explain the rationale behind China's OFDI, China's OFDI policies and the potential influence of China's OFDI in host countries. Regulation Theory was initially proposed by R. Boyer and other French Scholars (Jessop, 1990). It has been rekindled by a new generation of researchers gathered at the *Revue de la Régulation*, created and directed by Thomas Lamarche. Apart from Regulation Theory, the research result will also allow us to reflect the concept of "compressed development", developed by Whittaker et al. We expect to have a better understanding on how China's OFDI development may diversify the country's development path, different from other industrialized countries.



The time frame for analysis is set from 2000 to 2020. The data will be derived mainly from China's Ministry of Commerce, the ASEAN secretariat, International Monetary Fund, Aid data, AEI China investment tracker and the United Nations. As there is a gap in data collected from different sources, this research project will sort out the reasons behind the different OFDI numbers and come up with a new way to understand China's OFDI. Although China's OFDI is not a new research topic, there is still a lack of detailed analysis about China's OFDI in Southeast Asia in literature.

With the examination of this empirical study, this project also intends to contribute to the development of Regulation Theory.

There are three analytic dimensions in this research project. First, we will explore China's OFDI in Southeast Asia in terms of scale, breakdown of industry and host country. We will also examine China's motivations for OFDI by analyzing the evolution of its OFDI-related policy. The empirical study of China's OFDI in Southeast Asia will be compared with regulation theory and mainstream academic debates in international relations.

Second, we will investigate China's OFDI in detail through examining the investment in four specific sectors, including mining industry, transport & infrastructure, light manufacturing and financial services. These four sectors are also key in China's economic development. We will have better understanding on how China's OFDI contributes to its development through analyzing China's OFDI in these four sectors. This sectoral distribution can be compared with China's OFDI in other parts of the world and articulate the particular role of Southeast Asia in China's global OFDI strategy.

Third, we will analyze China's OFDI in four specific countries, including Singapore, Vietnam, Cambodia and Malaysia. The different level of industrialization and various capitalism development in these four countries provides a comparative angle in assessing China's OFDI in the region. These host countries' reactions and policy adjustment in the face of China's growing OFDI is also examined.

In sum, China's FDI in Southeast Asia has been growing the fastest among all regions in the world. The research will draw on EAI's research experience and network in China and EAI and UP's knowledge of economies in Southeast Asia. It will use an analytical framework developed by R. Boyer (research adviser) and Thomas Lamarche (PI) and apply this to the China-Southeast Asia relations. It will make use of data from various sources that provide a detailed breakdown of China's FDI in the region.

The proposed research is part of a broader research agenda, which EAI and UP have been jointly pursuing. Apart from China's OFDI, we will continue to investigate China's economic ties with Southeast Asia through other financial channels (eg; financial aid, China's RMB circulation in the region etc) in the years to come. The impact of China's OFDI on Southeast Asia's capital accumulation will also be our research topics in the future. This UP-NUS research grant will provide the first impetus to facilitate our joint research work and consolidate our long-term partnership.

SCIENCES PO (LIEPP)

Climate action plans inventories : policy instruments to reduce GHG emissions at the city level (CAPIInGHG)

The CAPIIn GHG project (Instruments for Climate Action Plans Inventories: reducing GHG emissions at the city level) is a 24 months project seeking to examine the selection, uses and effects of GHG inventories in cities in South East Asia and in Europe. Drawing on comparative public policy research, it combines a multilevel analysis of the changes taking place within national case studies and in a context where cities have become significant stakeholders and major drivers for implementing environmental ambitions. Bringing together the knowledge and expertise of LIEPP (Sciences Po & UP) and IESP (LKYSPP, NUS), the CAPIIn GHG project sets out to achieve the following objectives : 1) To assess the disconnect between ambitious environmental policy objectives and the way they are made material through local climate plans and the selection of GHG inventories, 2) To account for the disruptive impact resulting from the setup of new services (e.g., distributed energy), technologies (e.g., H2, electric mobilities) and stakeholders (e.g., global platforms, development entities such as AIIB) and the extent to which GHG inventories account for it; 3) To examine evolving environmental policy capacities (whether national or local) in relation to setting local climate action plans and select and adjust GHG inventories; 4) To carry out this research in a research framework comparing Asian and European cities, to account for main differences and similarities in local climate action plans and GHG inventories and contribute to current debates about regional policy styles.

The CAPIIn GHG Project will provide an assessment of the design and implementation strategies of policy makers in relation to a complex science-based instrument that has far reaching consequences in terms of accelerating vital city processes such as energy transitions, transport modernization and real-estate development. The variations observed and commonalities found should, in particular, point to the limits of these policy transfers and the embedded nature of these instruments, that while aimed at reducing CO2 levels, may operate along other specific sectoral logics. Second, it will contribute to current academic debates about persisting regional policy styles in mapping GHG emissions and addressing the climate emergency, while at the same time assessing standardizing dynamics resulting from the circulation of policy instruments and solutions through global policy communities and networks.

These findings will lead to a joint publication - edited book in a major university publisher or a special issue - including the contributions generated during the project time span and to a series of in-depth city monographs that will be used for local and international dissemination of the research. The CAPIIn GHG project also provides a unique opportunity for joint collaboration between two institutions currently engaged in a major restructuring of their environmental research and teaching activities.