

Dynamics of biological systems: emergent phenomena at different scales

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Book of Abstracts

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Neural Networks / 1

Kinematics of mice reinforcement learning in intelligent cages

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To study learning processes on behavioral level various experiments are performed on animals. In the last two decades several intelligent cages have been designed to increase throughput of such experiments. In my talk I will focus on Intellicage system where up to 14 mice can be housed and various learning protocols can be studied. I will propose a conceptual and computational framework combining point processes with reinforcement learning that can be used to describe the mice behavior as measured including learning and social aspects.

Patterns in Biology / 2

Stability of gene expression patterns in developmental systems with dynamic morphogen sources

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In developmental systems cells determine their fate by decoding chemical signals, called morphogens. This results in the emergence of gene expression patterns. I will address the problem of gene expression patterns stability in the systems where two interacting and diffusible gene expression products control the size of their own source regions. Such systems are encountered in e.g. spinal cord development, limb formation and many others. The reaction-diffusion equation with threshold-activated production term is employed as a generic model for this problem. It is found that its dynamics is governed by the conservation law, which leads to a range of analytical results. In particular, phase transition is observed, between the phase of indeterminate patterning, where the region of mixed gene expression is ever growing, and the phase of travelling gene expression patterns, where two expression domains form a well-defined contact zone. A sub-class of genuinely stationary patterns is then identified, alongside the exact conditions ensuring this stability. These results allow me to classify all one- and two-gene regulatory motifs by their ability to produce stable patterns.

Complexity of Life / 3

Human adaptations for extreme environments during simulated space analog missions

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Living organisms possess natural ability to adapt in response to changing environmental conditions. Limitations in adaptation are critical in strategies of survival. Simulator of space base located in Rzepiennik in Poland is an isolated laboratory established in 2018 to run studies in bioastronautics and space medicine. During each year international crews of maximum six people enter the isolation for 7 days, where they undergo detailed monitoring and examination of physiological, psychological, and cognitive parameters using non-invasive measurement methods. Until now, the data base contains results from more than 250 participants, which is the largest such data base in the world.

Collected data can be processed in multiple ways to create predictive models of human behavior, for example to mitigate risks, to improve team work, to detect novel group dynamics phenomena, to optimize crew composition in realization of critical projects, to evaluate human performances and many others.

This presentation focuses on analysis of human adaptation in controlled extreme environment which is based on isolation from sunlight; altered time perception; confinement; limited access to food, water, electricity and internet; elevated levels of carbon dioxide; sleep deprivation; oversaturated workload and stressful emergency simulations.

Complexity of Life / 4

Computational modelling approach of nonlinear signalling networks in the fish endocrine system (CANCELLED)

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The hormonal communication networks between the brain (notably the hypothalamus-pituitary complex) and the peripheral glands (such as the gonads) build up the dynamic endocrine signalling pathways of the aquatic lower vertebrates, especially fish. The neuroendocrine controller involved in this circuitry can be effectively reduced to the hypothalamic-pituitary-gonadal (HPG) axis. In the classical HPG axis, the gonadotropin releasing hormone (GtRH) is produced in the hypothalamus, which reaches the pituitary gland to stimulate the gonadotropins, such as the follicle stimulating hormone (FSH) and the luteinising hormone (LH). These hormones regulate the steroidogenesis in the reproductive system, however, the fully quantitative and mechanistic understanding on the fish HPG dynamics has not yet been achieved.

In this presentation, a computational framework is shown as a model for the signalling pathway that governs the neuroendocrine dynamics of HPG axis in fish. A nonlinear system of ordinary differential equations was constructed to represent the metabolic networking structure. We analytically solve the equations to obtain approximate solutions for predicting the time-varying behaviours of the hormone (FSH and LH) biosynthesis in the fish HPG axis, by assuming environmentally relevant situations that affect the GtRH signalling. This theoretical model enables the quantitative data analysis and mechanistic prediction of the reproductive pharmacokinetics of fish in the context of comparative physiology.

Complexity of Life / 5

Emergent Robustness from Multiple Timescale Adaptive Dynamics

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Biological and neural networks are adaptive - their connections slowly change in response to the state of the coupled elements making up the systems. The dynamics of such adaptive networks are intriguingly complex, rendering it extremely difficult to answer the fundamental question of what the energy requirements for maintaining functionally robust collective states under environmental stochasticity are. Aiming to understand the essential role of free-energy consumption in robust adaptation, a basic problem in evolution and learning, we introduce a new framework based on path-integral formalism in non-equilibrium statistical physics. As a specific example of our theory, we apply it to biological evolution, where phenotypes are shaped by gene-expression fast dynamics that are subjected to an external noise while genotypes are encoded by the configurations of a network of gene regulations. This network slowly evolves under natural selection with a mutation rate, depending on how adapted the shaped phenotypes are. Here we establish a relation between the averaged entropy production rate (EPR) and the evolutionary speed which is quantified by the genetic variance. Specifically, EPR is shown to increase with increasing evolutionary speed at a low noise level, while a robust gene-expression pattern is maintained within an intermediate level of noise at a much lower value of EPR. The emergence of such robustness as well as its associated EPR can be characterised analytically within our framework as the onset of instability of the attractor state with zero gene-expression levels.

Complexity of Life / 6

Effects of toxicity and zooplankton selectivity under seasonal pattern of viruses with time delay on plankton dynamics

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A mathematical model for the interacting dynamics of phytoplankton-zooplankton is proposed. The phytoplankton have ability to take refuge and release toxins to avoid over predation by zooplankton. The zooplankton are provided some additional food to persist in the system. The phytoplankton are assumed to be affected directly by an external toxic substance whereas zooplankton are affected indirectly by feeding on the affected phytoplankton. We incorporate seasonal variations in the model, assuming the level of nutrients, refuge and the rate of toxins released by phytoplankton as functions of time. Our results show that when high toxicity and refuge cause extinction of zooplankton, providing additional food supports the survival of zooplankton population and controls the phytoplankton population. Prey refuge and additional food have stabilizing effects on the system; higher values of the former results in extinction of zooplankton whereas phytoplankton disappear for larger values of the latter. We find that time delay accounts for recurrent stability switching event in the system. Seasonality in nutrients level and toxins released by phytoplankton generates higher periodic solutions while time-dependent refuge of phytoplankton causes the occurrence of a period-three solution. The possibility of finding additional food for zooplankton may push back the ecosystem to a simple stable state from a complex dynamics.

Patterns in Biology / 7

A Clock and Wavefront Self-Organizing model explains somitogenesis in vivo and in vitro

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During mouse development, presomitic mesoderm cells synchronize Wnt and Notch oscillations, forming sequential waves that pattern somites. Classical somitogenesis models attribute these synchronizations to global morphogen gradients. However, increasing evidence suggests that they could arise in a self-organizing manner. Here, we introduce the Sevilletor, a novel reaction-diffusion system that serves as a framework to compare different somitogenesis hypotheses. Using this framework, we propose the Clock and Wavefront Self-Organizing model, the first somitogenesis hypothesis where phase waves are formed by a guided self-organizing process. Our analysis shows that this model can recapitulate the formation of multiple phase waves observed upon ectopic expansion of posterior gradients. Moreover, it can explain the formation of circular phase waves observed in explants that lack global signals. Finally, it provides a theoretical basis for understanding the excitability of mouse presomitic mesoderm cells and the changes in relative phase of Wnt and Notch observed during mouse somitogenesis.

Complexity of Life / 8

Complexity flow graphs

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Evolution of biological complexity seems to be a great puzzle. Although the extended evolutionary synthesis and modern technology provide a wide range of theoretical models and practical tools to study evolutionary dynamics [1][2], evolution of complexity is usually omitted. Moreover, some researchers propose that complexity can be treated as the byproduct of evolutionary adaptation [3]. For this reason it is important to develop new tools and methods to study complexity dynamics in evolution.

Inspired by the Maxwell's Demon, the Demonic Selection Principle states that the complexity of the population of organisms cannot be greater than complexity of all selective filters acting on it [4]. Although the principle itself can be questioned, the upper complexity limit is thought to be dynamic. For example, the population itself may permanently change its own environment that in consequence leads to distortions of selection pressures, creating a feedback. However, the relation between selection forces and the complexity of adapting population remains vague.

For this reason, a new method to study evolution of complexity was created, i.e., complexity flow graphs. The graphs try to track dynamics of evolving population complexity by estimation of changes in biocomplexity and complexity of selective filters that shape it. The comprehension of relative changes between these complexities may shed more light on the evolution of complexity. Complexity flow graphs were created based on a model incorporating 1D cellular automata inspired by a process of evolution with niche construction.

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Neural Networks / 9

Exploring Dendritic Plasticity: How Synaptic and Ion Channel Adaptations Enable Single Neurons to Rival Artificial Neural Network Complexity

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In the traditional view, we often see a single neuron as less computationally efficient than a multilayer artificial neural network. But is this truly the case? Our investigation delves deep into the computational efficiency of morphologically complex neurons, especially their ability to distinguish between different synaptic patterns. We posed a question: What is the simplest dendritic structure that can master tasks usually reserved for multilayered artificial networks? This exploration not only challenges long-held beliefs about single neuron capabilities but also bridges the gap between biological and artificial neural computation. Furthermore, building upon the foundational homeostatic models pioneered by Eve Marder, we introduced an enhanced model tailored for morphologically complex neurons. Central to our method is the fine-tuning of diverse ion channel composition throughout the whole dendritic tree, ensuring a good balance of homeostatic activity. Our findings reveal that training to recognize synaptic patterns and the homeostatic tuning of ion channels can be unified under one computational strategy. This perspective encourages a more holistic understanding of dendritic tree adaptation, encompassing both synaptic and ion channel modifications. In essence, our study offers a fresh lens through which to understand neuronal learning, merging the worlds of artificial and biological neural networks.

Complexity of Life / 10

Pandemic and post-pandemic mobility and contact patterns in Berlin - preliminary results

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The COVID-19 pandemic has clearly shown how unprepared we are globally to adapt and manage effective public health responses in urban context. This pandemic has not only transformed how people navigate urban spaces but also how they physically interact with each other. This study aims to understand these changes in Berlin by utilizing GPS mobile phone data from 2020 and 2022 and performing a comparative analysis of mobility patterns during the pandemic and post-pandemic periods. In particular we study the month of November for each year to minimize external influences, during which we observed significant shifts in human mobility and interactions. Our dataset includes 72,301 records (contacts) among 14,908 mobile phones (individuals) in 2020, and 96,844 records among 11,094 individuals in 2022. Contacts between individuals were recorded when mobile phones were within an 8-meter distance for a minimum of 2 minutes. Our methodology encompasses a range of approaches, including examining the cluster and community structure of the contact network, exploring motifs in how people move between common settings (home, work, and others), and investigating the heterogeneity of people's activities. Using social network analysis, we were able to reveal a change in mobility patterns, with the average nearest neighbor distances being

less path-like during the pandemic compared to the post-pandemic period. However, the frequency of motifs remained similar across both periods. This study not only reveals the immediate impact of the pandemic on urban mobility and contact patterns but also contributes to the improvement of response strategies in future crises.

Patterns in Biology / 11

From cell mechanics to tissue-scale properties properties in development

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The developmental process implies precise but significant changes in the geometry and structure of the embryonic tissues. Recent results show that apparently minor changes in the mechanical properties at the cellular level trigger deep, non-linear transitions in the topological organization of the whole embryonic tissue. In consequence, the tissue changes its material properties abruptly, enabling or preventing geometrical deformations. Open questions remain, like the potential existence of causal feedbacks between cell differentiation processes and the potential heterogeneity of topological patterns existing within the tissue. The results presented in this talk are based on the fundamental assumption that predictive frameworks in theoretical biology must explore the connection between different scales of the system. In this particular case, we use topology to establish a bridge between the system's scales defined by i) the cell level and ii) the cell collective/tissue level. Establishing this connection enables us to predict global, non-trivial behaviours in tissues from the empirically feasible observables related to the mechanical properties of single cells.

Complexity of Life / 12

The tale of the mouse and the fly: Biophysical modeling, optimization and inference for elucidating distinct developmental strategies

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For different organisms, early development unfolds under very different circumstances and time scales, but constantly facing the impacts of inevitable biological noise resulting from the inherently stochastic nature of the processes driving it. To cope with this, a variety of developmental strategies and mechanisms evolved, and their differences were shaped by the constraints imposed by physical laws and the natural environment of the organism. In spite of decades of research on early development of various paradigmatic organisms, we are still lacking theories and models that explain these processes in a truly mechanistic fashion. The advent of increased computational power has enabled us to construct developmental models with ever increasing complexity. However, since experimental reports on microscopic cell-physical quantities are scarce, the parametrization of such models becomes a key problem itself and posits a new frontier in biophysical modeling. In this talk, I will contrast two distinct strategies for parametrizing biophysically realistic models in development and beyond: optimization of normative theories, and Bayesian inference, which in principle can operate even in a model-free regime. I will first demonstrate that both approaches can be unified into a single mathematical framework which allows smooth transition between both strategies in a quantitative way. I will then present our results on elucidating early development of two distinct organisms while making use of both strategies of parametrization: (1.) optimization of a detailed spatial-stochastic model of the gap gene system in the fruit fly, and (2.) characterization of the spatial regulatory processes driving early cell fate assignment in the preimplantation phase mouse embryo

via SBI (simulation-based inference), a powerful recent AI-based inference toolkit. These results exemplify how optimization of normative models and inference or fitting strategies can be combined for successfully determining complex spatial-stochastic models, and at the same time highlight that significantly different developmental strategies emerged under the vastly different circumstances faced by the fly and mouse embryos.

Patterns in Biology / 13

Mathematical modelling of cancer invasion: Phenotypic transitioning provides insight into multifocal foci formation

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The transition from the epithelial to mesenchymal phenotype and its reverse (from mesenchymal to epithelial) are crucial processes necessary for the progression and spread of cancer. We investigate how phenotypic switching at the cancer cell level impacts the behaviour at the tissue level, specifically on the emergence of isolated foci of the invading solid tumour mass leading to a multifocal tumour. To this end, we propose a new mathematical model of cancer invasion that includes the influence of cancer cell phenotype on the rate of invasion and metastasis. The implications of the model are explored through numerical simulations revealing that the plasticity of tumour cell phenotypes appears crucial for disease progression and local invasive spread [1]. The computational simulations show the progression of the invasive spread of primary cancer reminiscent of in vivo multifocal breast carcinomas, where multiple, synchronous neoplastic foci are frequently observed and are associated with a poorer patient prognosis.

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Complexity of Life / 14

Pattern formation during social contagions: epidemics, infodemics and civil unrest

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Social contagions unfolding over time and affecting large populations show intricate spatiotemporal dynamics which are driven by complex human behaviours and population mobility. These contagions may vary in their type, ranging from pandemics to infodemics, and from opinion polarisation to civil unrest. We will examine the impact of behavior-dependent mobility on the contagion spread within a unifying framework which is based on the Maximum Entropy Principle, Lotka-Volterra dynamics and methods of percolation theory. Complex patterns formed by the contagion spread will be mapped into Turing patterns typically observed in reaction-diffusion systems. We will characterise the resulting pattern formation in terms of phase dynamics, highlighting phase transitions between distinct configurations, and argue that the identified critical regimes imply that small changes in individual risk perception could lead to abrupt changes in the spatial morphology of the contagion phenomena.

Neural Networks / 15

Cholinergic modulation of neuronal excitability underlies differential dynamics and roles of NREM and REM sleep during sleep dependent memory consolidation.

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Across vertebrate species, sleep states are known to cycle consistently from non-rapid eye movement (NREM) to REM sleep. However, the functional significance of these transitions is unknown. We use a simplified biophysical network model to show that state-specific changes in cholinergic signaling during NREM and REM sleep can mediate dramatic changes in network dynamics and subsequently can play differential and critical role in sleep dependent memory consolidation. Specifically, we show that the sequential, bidirectional changes in cholinergic neuromodulation during these sleep states plays a vital role in memory consolidation, particularly when multiple memory traces are being stored simultaneously. The low-ACh (NREM-like) state, mediates rapid recruitment of new cells into the memory engram, and their consequent enlargement, while subsequent high-ACh (REM-like) state suppresses activity among newly recruited excitatory pyramidal neurons during prior NREM, leading to the orthogonalization of newly enhanced representations of different memory traces. We further find that, this iterative sequence of state-specific network dynamics is essential for memory storage in the network.

Neural Networks / 16

About hierarchical correlation reconstruction, multi-feature Granger causality, and others

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While machine learning is usually focused on prediction of values, on various applications I will introduce to simple family of methods to work with learned probability distributions - e.g. model joint, predict conditional, their time evolution. One proposed application direction will be multi-feature Granger causality, enhancing the standard method with evaluation of propagation speed, and automatic extraction of multiple types of dependencies for example in EEG data. There will be also proposed its application to build artificial neurons updating model of joint distribution of its connections.

Neural Networks / 17

Fractal and multifractal organisation of neuroimaging signals in cognitive tasks and in disease

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In this contribution, we present A) a detrended fluctuation analysis of functional magnetic resonance imaging (fMRI) data from a working memory experiment and B) a multifractal analysis of the electroencephalography (EEG) data obtained from patients with multiple sclerosis (MS). fMRI and EEG signals are notoriously challenging to analyse due to their very low temporal and spatial resolution, respectively, and a non-trivial auto-correlation and cross-correlation structure.

In A), we applied fractal analysis to investigate how a person is memorising and retrieving information in four types of experimental tasks: two visual-verbal (based on lists of semantically or phonetically associated words) and two non-verbal (pictures of similar objects). The regional brain activity was quantified with the Hurst exponent (see Fig. 1) and Detrended Cross-Correlation Analysis (DCCA) [1,2].

We clearly observe $1/f$ signature in most brain areas, a reduction of persistent behaviour in tasks relative to the spontaneous brain activity and regional dependence of exponents depending on the tasks and the stage of the experiment (memorising the stimuli or information retrieval). We uncover such regionally coordinated changes also by analysing eigensystems of detrended correlation matrices (which turn out to be more sensitive than Pearson correlations).

In B), we compared the complexity of the EEG time series, paying particular attention to analysing the correlations between the degree of multifractality, disease duration, and level of disease progression quantified by the Expanded Disability Status Scale (EDSS). We used Multifractal Detrended Fluctuation Analysis [3], a generalisation of the DFA which is a robust tool for multilevel characterisation of time series (e.g., see [4]) and specifically other types of brain signals [5]. Based on the generalised Hurst exponents, we obtained the multifractal/singularity spectrum of the Hölder exponents [6], $f(\alpha)$. To quantify the coupling between the brain regions we again used the DCCA.

Our results reveal a significant correspondence between the complexity of the time series and the stage of multiple sclerosis progression. Namely, we identified brain regions whose EEG signals were characterised by a well-developed multifractality (the estimated multifractal spectra take the shape of asymmetrical parabolas with larger widths $\Delta\alpha$) and lower persistence of the time series (spectra localised above but closer to $\alpha=0.5$) for patients with a higher level of disability, whereas for the control group and patients with low-level EDSS they were characterised by monofractality and higher persistence. The link between multifractality and disease duration has not been observed. Our conclusions are supported by the cross-correlations analysis.

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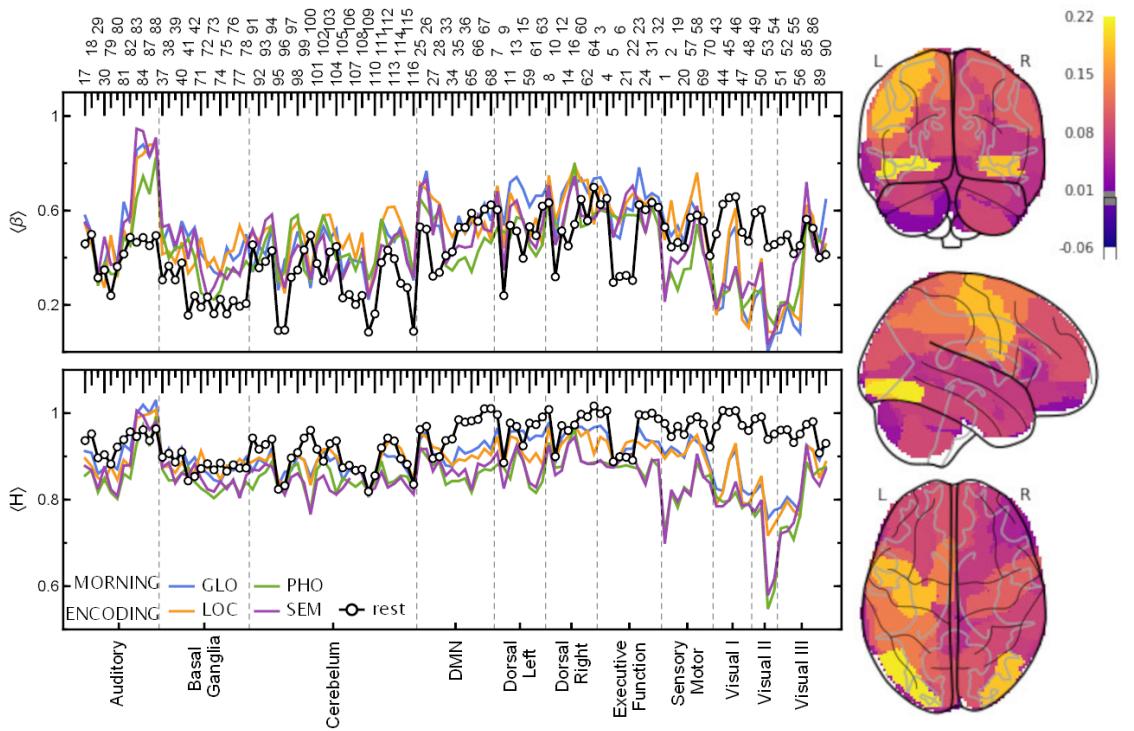


Figure 1: Fig. 1

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Novel studies of cancer cells heterogeneity

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The phenomenon of cellular heterogeneity - the presence of diverse subpopulations in the cell lines cultures - is the subject of many recent studies. This effect is especially pronounced in the cancer cells populations which, in turn, can influence the outcome of anticancer therapies. It is postulated that heterogeneity is the result of long term evolution of cell types. However, heterogeneity also can be seen in the short term changes in the properties of cell populations. Here, it will be shown that the heterogeneity is a highly dynamic event and that it depends on mechanical properties of cellular microenvironment in the case of migrating WC256 Walker carcinosarcoma cells. This can help to understand a dynamics of cancer cells behavior which in turn may improve cancer therapies.

Neural Networks / 19

Mapping Brain Connections: The Role of Relaxin 3/RXFP3 system in Behavior and Functionality

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Understanding connections in the brain at one major neurotransmitter level provides us with detailed information from the molecular scale to behaviour and functionality.

The Relaxin 3/RXFP3 system plays an important role in the modulation of emotional and behavioural actions, such as arousal, regulation of appetite, sociability, stress, anxiety, memory, sleep, and circadian rhythms. The major source of the relaxin 3 peptide is the nucleus incertus (NI), a pontine structure located near the fourth ventricle. The NI projects throughout the brain, and one of the most important connections is the septohippocampal pathway.

Methods used in research that aims to map these pathways involve antero- and retrograde viruses (AAV) or fluorodyes. They are respectively used during stereotactic operations. For example, AAVs contribute to the expression of fluorescent proteins such as YFP, GFP, or mCherry, which can later be imaged in a fluorescent microscope. Specific antibodies can also be used to identify precise types of neurons.

Understanding the relevance and course of the relaxin 3/RXFP3 pathways, as well as the placement of fibres containing this neuropeptide or the RXFP3 receptor, contributes to behavioural research, confirming its significance in social behaviour, depression, and further pathology in Alzheimer's disease

Complexity of Life / 22

Health risks of human space exploration

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For almost 60 years, human beings have been flying to the outer space, successfully completing missions in order to expand our knowledge about the universe. Over those years, we also have gained a lot of experience about the risks of human space flight. In the forthcoming perspective of the end of the International Space Station (ISS) service, international space agencies urge to plan the next step of human space exploration beyond LEO. They are aware of additional health risks of exploration class missions to the Moon and beyond. Far away from Earth, astronauts will be exposed to hostile environment, changed gravity fields, confinement, and ionizing radiation, which has been recognized as no. 1 risk of human spaceflight in exploration class missions. As in the future human beings will travel to deep space, extraordinary means will have to be taken to safeguard astronauts on the way to the Moon. During long duration deep space missions humans will experience different doses and spectra of ionizing radiation than on the International Space Station, posing new, detrimental-level risks to living organisms during and after exposure to space radiation environment. International Space Agencies have already recognized the necessity to better understand the effects of space radiation to the human body, in order to estimate the health risk and predict the consequences of long-duration space flight, including European Space Agency, where the Space Medicine Team at the European Astronaut Centre has been working towards understanding, predicting and reducing potential hazards for astronauts during deep space missions. Here, a summary on health risks of human spaceflight is presented, with emphasis on biological effects to the human body, that may occur due to ionizing radiation in the deep space environment. Current strategies for health risk assessment are shown, as well as the challenges for risk predictions of long-duration deep space missions.

Complexity of Life / 23

Self-Organization of Lifelike Behaviours

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Life is a multifarious bundle of distinct physical phenomena that are distinctive, but not unique to, living things. Self-replication, energy harvesting, and predictive sensing are three such phenomena, and each can be given a clear physical definition. In this talk, we will report recent progress in understanding what physical conditions are required for the spontaneous emergence of these various lifelike behaviours from assemblages of simple, interacting components.