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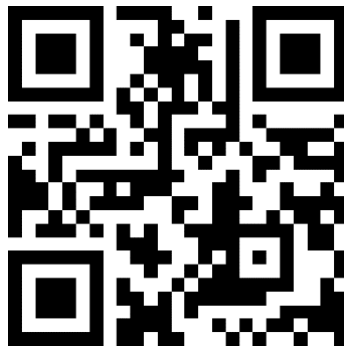


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"Human and artificial intelligence in science and society"

BOOK OF ABSTRACTS



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DIGITAL HUMANITIES, AI, AND HIGHER EDUCATION

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The current intensified state of technological development is substantially changing the research environment in every direction of scientific research. The seemingly conservative field of Humanities is no exception. In fact, historical research seems to be one of the fields closest to proving that Digital Humanities are already entering a new stage of evolution. Partners from Humanities and Computer sciences are not just borrowing data and methods from each other but seem capable of formulating new methods, questions, and, ultimately, knowledge.

This presentation will focus on several projects (ACCSN, DigiThrace, DigiDeultum, GKRP, CN, D4N4, and Thracian Rider database) exploring the possibilities of conducting research and re-visiting traditional historical questions in an innovative digital environment. Moreover, a specific accent will be put on the ways of transmitting and actively applying this new, rapidly developing know-how in higher education, with a particular focus on historical research of Antiquity and the Middle Ages. A key question becomes: How should future researchers be educated to explore past human societies in their political, economic, social and cultural context through digital tools and AI?

ON THE INCREASING ROLE OF AI IN THE BIOMECHANICS OF HUMANS

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The intersection of artificial intelligence (AI) and biomechanics has brought about significant advancements in the field of human movement analysis, rehabilitation, and sports performance enhancement. Biomechanics, the study of the mechanical aspects of living organisms, has a wide range of applications including understanding human movement, designing prosthetic devices, and optimizing athletic performance. The integration of AI technologies in biomechanics has led to the development of sophisticated tools and techniques for data analysis, predictive modeling, and personalized interventions.

One of the key areas where AI has made a substantial impact in biomechanics is in human movement analysis. Traditional biomechanical analysis involved time-consuming manual processes for tracking and interpreting movement data. However, AI algorithms have revolutionized this process by enabling automated tracking and analysis of complex movement patterns.

AI has proven to be instrumental in the development of advanced prosthetic and orthotic devices. By utilizing AI-powered control algorithms and sensor technologies, prosthetic limbs can now adapt to the user's movement patterns and provide a more natural and biomechanically efficient gait. These systems employ pattern recognition and predictive modeling to anticipate the user's intent and adjust the device's behavior in real time. As a result, individuals with limb loss or limb impairment can experience improved mobility and comfort, ultimately enhancing their quality of life.

In the realm of sports science, AI has been leveraged to optimize athletic performance and reduce the risk of injury. By analyzing biomechanical data from athletes, machine learning algorithms can identify movement patterns associated with optimal performance and injury prevention.

Finally, let us mention that as with any modern technology, together with the advantages which it brings with itself, it involves also some risks. Part of them is related to privacy and data security related on handling sensitive patient data. This demands robust privacy measures. Ensuring compliance with ethical standards and data protection regulations is also critical. In this respect, one shall obey the guidance of the corresponding document on the ethics and governance by the World Health Organization on AI. It is based on the collective views of experts in public health, medicine, law, human rights, technology, and ethics.

ELEMENTS OF AI IN COMMERCIAL PRODUCTS FOR PHYSICS SIMULATIONS

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One of the directions of the current development of the commercial products for physics simulations is to simplify the work of the users. Many operations – like creation of the mesh for the numerical solution of the differential equations – in the past were performed by the users. Now this is done by the product choosing optimal parameters for the solved problem. Also the choice of the best solver for the problem is done by the product.

Another example for elements of AI is the analytical solution of equations or integrals. For the moment commercial products for simulations and mathematics are better in this field compared to ChatGPT.

A key question from educational point of view is how to change the curriculum and teaching of the students in order to prepare them for effective application of the new tools related to the AI. Some other aspects of the digitalization of the education are also discussed in the presentation.

ARTIFICIAL INTELLIGENCE AND WORKPLACE INNOVATIONS

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Modern information technologies and systems with elements of artificial intelligence change the working world: labour markets, work organisation, work tasks and processes, contribute to the emergence of new work models such as hybrid work models and platform work, reveal new opportunities for self-employment, and change the profile of the necessary competencies of personnel. Technological solutions with artificial intelligence replace specialists in the implementation of part of the work tasks and allow their faster and more precise execution. Automation of work tasks covers more than the physical actions of operating machines and repetitive tasks. Artificial intelligence enables the performance of non-routine mental tasks, if the computerised system can derive a logical pattern of dependencies such as data collection and processing activities and algorithmic process control. Despite technological advances, man cannot be replaced in the performance of a number of work tasks that are part of various professions.

The digital transformation of work contributes to a change in the culture related to the attitude to work and work values which affects the relationship “security – flexibility in the workplace”, combining work and private life, career development, interaction “person – robotic technologies”, subjective perception of quality of work.

The models of work based on the potential of modern information technologies in labour activities create challenges for business organisations. Solving these challenges involves combining technological innovation with social innovation. In this sense, the present report addresses the debatable and insufficiently researched question of what changes in managerial and social terms should be accompanied by the application of digital technologies and systems with artificial intelligence in labour activities in order to achieve efficiency and higher quality of work. The subject of research is the potential of information technologies for innovative renewal of jobs in business organisations. The report contains a literature review of the high-quality contributions that analysed different aspects of the innovation potential of digital technological solutions and artificial intelligence for transforming work processes, tasks and work practices in the organisation. The author’s point of view on the concept of workplace innovation is presented and its role in conditions of accelerated digitisation of labour is discussed. Conclusions and recommendations from the research are formulated.

MATHEMATICAL SOCIAL DYNAMICS AND ARTIFICIAL INTELLIGENCE

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In this presentation, we discuss two applications of mathematical methodology to model the phenomena from the area of social dynamics: motion of migrants in a channel of migrant network and a model of epidemic spread. We present the corresponding models and discuss how the methods of artificial intelligence can be used to support such kind of models.

References

1. Vitanov, N. K., Vitanov, K. N. (2023). Epidemic waves and exact solutions of a sequence of nonlinear differential equations connected to the SIR model of epidemics. *Entropy*, 25(3), 438.
2. Vitanov, N. K., Borisov, R., Vitanov, K. N. (2021). On the motion of substance in a channel and growth of random networks. *Physica A: Statistical Mechanics and its Applications*, 581(C).

SOCIAL THERMODYNAMICS 2.0

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Thermodynamics is the most general quantitative theory for description of complex systems, dealing with simple mathematics in an elegant way. The First Law of thermodynamics recognizes energy conservation. The Zeroth Law reflects transitivity of thermodynamic equilibrium and introduces temperature as a unique intensive parameter, which becomes uniform in the entire system at equilibrium. The Third Law restricts temperature positively. Its conjugated extensive variable is the entropy, which is ruled by the Second Law governing the direction of spontaneous processes in Nature. Entropy is a key concept in science as a measure of uncertainty, originating from lack of complete knowledge for the studied systems and phenomena. A typical example is classical thermodynamics, where thermal entropy was an icon of the technological revolution (1870-1920). Statistical mechanics entropy symbolized the scientific-technical revolution (1920-1970), while information entropy was an essential part of the digital revolution (1970-2020). Currently the intelligence revolution (2020-2070) is taking place, where social entropy must play a central role. Because thermodynamics is a macroscopic theory, the underlying microscopic dynamics is hidden from the observer. It is not lost, however, and the entire unknown mechanical information builds up the entropy, a measure of disorder being absent in mechanics. The hidden information is not equally important to entropy and quantum Darwinism is a way for selecting the mechanical information essential for thermodynamics. The four fundamental Laws above are the summit of thermodynamics, and the entire subject is application of the basic principles particularly to solve problems. Recently such social applications emerged as Thermodynamics 2.0, which may soon become a central part of the more general sociophysics and econophysics.

Trailing the modern ideas of sociophysics a minimalistic thermodynamic model of society is proposed [1], which consists of three social ingredients: people, economy, and entropy. Employing the universal van der Waals equation of state, many important relationships are discovered, including laws of econophysics. A paramount finding is that the Second Law of thermodynamics governs irreversible social evolution, revealing the power of social liberty and economic freedom.

References:

[1]. R. Tsekov, *Social Thermodynamics 2.0*, arXiv 2307.05984 (2023)

AI IN EXPERIMENTAL NUCLEAR PHYSICS?

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Artificial intelligence (AI) is participating more and more in our daily life. We could find the algorithms of machine learning (ML) in every field. Can we apply the ML methods into researches in nuclear physics?

We can use the AI in radiation protection, data analysis and model predictions. AI is increasingly integrated in radiation medicine. With AI we can develop algorithms that can improve the safety of personnel and the public, based on previous results. AI can be used and for the data analysis from nuclear experiments and for the better understanding of the nuclear forces and the interpretation of the results. Implementation of AI and ML methods would significantly benefit safeguards by increasing the efficiency of these activities.

MACHINE LEARNING AND ARTIFICIAL INTELLIGENCE IN THE APPLICATIONS OF THE ENVIRONMENTAL FLUID MECHANICS

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Abstract: Over the last few years, machine learning (ML) has been implemented in most social, scientific, engineering, and industry branches, setting up the point where computer and statistical science meet. ML evolution has been driven by advancements in Artificial Intelligence (AI) and its related algorithms.

The application of Machine Learning (ML) and Artificial Intelligence (AI) in the domain of environmental fluid mechanics is nowadays the latest trend in fluid mechanics and has shown promising advancements in understanding, modeling, and optimizing fluid flows. This analysis provides insights into the application of ML and AI techniques in various aspects of fluid mechanics, highlighting their potential, limitations, and future prospects.

Both ML and AI are increasingly being applied in the field of environmental fluid mechanics to address complex problems and improve predictive capabilities.

This article discusses the status of artificial intelligence and machine learning in different fields in fluid mechanics and how they both can accelerate the process for achieving the goals in different fields in fluid mechanics development.

Keywords: Artificial intelligence, Machine learning, Data analysis, Fluid mechanics

MOTION OF RESEARCHERS BETWEEN RESEARCH ORGANIZATIONS: CAN AI HELP TO DIRECT THE PROCESS?

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We discuss a mathematical model of motion of a substance in a node of a network which has a structure consisting of a chain of cells. An exact solution for the model equations is obtained in the case when the structure of the node is a chain of two cells. The obtained general results are applied to the construction of a theory for the specific case of motion of young and experienced researchers between research organizations. We discuss how artificial intelligence can support the calculations connected to the model and the application of the results of the model to practice.

References

1. Vitanov, N. K., Dimitrova, Z. I. (2024). A Mathematical Theory of Motion of Researchers between Research Organizations. *Mathematics*, 12(13), 1984.
2. Vitanov, N.K., Dimitrova, Z.I. (2021). Remarks on Dynamics of Research Production of Researchers and Research Organizations. In: Manolopoulos, Y., Vergoulis, T. (eds) Predicting the Dynamics of Research Impact. Springer, Cham. https://doi.org/10.1007/978-3-030-86668-6_3

MATERIALS AND STRUCTURES FOR NEUROMORPHIC COMPUTING

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The idea of “neuromorphic” computing dated back in the early 1990s, when the researchers began to investigate the possibility to create brain-inspired analog computing devices. These devices should resemble the operation of human’s brain most important cell – the neuron. Neurons interact and communicate with one another thus forming neural networks (NN). This enables humans to think and more important – to learn. Neurons fire electric signals and communicate with other cells via synapses (neurotransmitters). There are significant differences between the conventional binary computing and neuromorphic analog computing, namely: sequential vs. parallel processing; separated computation and memory vs. collocated computation and memory; binary data vs. spikes communication. The unprecedented progress in CMOS technology resulted in impressive achievements in neuromorphic computing, e.g. biologically inspired chip “TrueNorth”, IBM that implements one million spiking neurons and 256 million synapses on a chip. However, it is several orders of magnitude more power intensive than the human brain. Therefore, new material and device concepts should be developed to outperform conventional CMOS based technology.

This talk will present the new materials and emerging memory concepts, which are currently investigated for the realization of compact circuits capable of emulating neuron and synapse functionalities. There are several major emerging memory technologies that hold the promise for neuromorphic computing - resistive random access memory (ReRAM), phase change memory (PCM), magneto-resistive random access memory (MRAM), ferroelectric random access memory (FeRAM). Increasing interest toward these novel device concepts results from their ability to store information at the nanoscale in an analogue and non-volatile way. The physical phenomena and operation principles as well as the materials and technologies to realize them will be presented.

QUANTUM CHEMICAL INVESTIGATION OF THE REACTION PATH OF COUMARIN DERIVATIVES

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Coumarins (2-oxo-2H-benzopyrans) represent a large class of natural heterocyclic compounds. Coumarins and their derivatives are of particular interest to modern organic synthesis and pharmacology due to their wide variety of biological activity. Dihydrodimers of coumarins, like the coumarin derivatives, are also biologically active compounds. Some of the representatives are widely used as laser dyes, fluorescent markers and calorimetric sensors.

By means of DFT calculations we aim to clarify the mechanism of dimerization of 3-acetylcoumarin and its derivatives. For this purpose, the relative stability and conformational interconversion of various intermediate states was calculated. The importance of the reaction conditions i.e., presence of metal (e.g. Zn) and metal salt in the reaction was also clarified and investigated.

The calculations were conducted, using hybrid exchange-correlation functional – B3LYP and basis set 6-31++G**, using Gaussian16 software package. For the calculations an implicit solvent PCM (THF) model was used. Further investigations were done using full atomistic model of the system, based on DFT. To evaluate the different intermolecular interactions in the system, the model includes the reactants, metals, metals salts, as well as the solvent used in the reaction mixture, in ratios accurately matching experimental data. The MD simulations were carried out using NVT ensemble, T=300 K, using cp2k simulation package.

References:

1. Kise, J. Org. Chem, 2006, vol. 71, 9203-9207
2. A. I. Koleva et. al, Molecules, 2019, vol. 24(11), 2030
3. K. Simeonova et. al, Molecules, 2022, vol. 27(21), 7228

BEAM SHAPING OF FEW-CYCLE LASER PULSES

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In this talk we will demonstrate the possibility to generate long-range quasi non-diffracting Bessel-Gaussian beams using highly-charged optical vortices. Moreover, we will show that spiral phase plates fabricated to ensure an azimuthal change of the accumulated phase of a multiple of 2π at a predetermined design wavelength, can be used in a broad spectral range around the designed wavelength. This means that high-quality long-range Gauss-Bessel beams can be successfully generated by using vortex phase plates designed for one wavelength, illuminating them with laser beams at much different (formally “inadequate”) wavelengths.

Based on this knowledge and the proposed technique we will show that even in the sub-8-fs range is possible to generate such high-quality Bessel-Gaussian beams without noticeable consequences for the measured pulse duration [3]. The obtained beams have diffraction half-angles below $40 \mu\text{rad}$ and reach propagation distances in excess of 1.5 m.

References:

- [1]. L. Allen, M. W. Beijersbergen, et al., Phys. Rev. A 45 8185–8189 (1992).
- [2]. L. Stoyanov, M. Zhekova, A. Stefanov, et al., Scientific Reports , vol. 10, 21981 (2020).
- [3]. L. Stoyanov, Y. Zhang, A. Dreischuh, and G. G. Paulus, Optics Express , vol. 29, 10997-11008 (2021).

WER HAT DAS GESCHRIEBEN? ÜBER DIE ENTSTEHUNG UND FOLGEN EINES TEXTES ÜBER DIE ZUFÄLLIGE ENTSTEHUNG SINNVOLLER TEXTE

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„Einst träumte Dschuang Dschou, dass er ein Schmetterling sei, ein flatternder Schmetterling, der sich wohl und glücklich fühlte und nichts wusste von Dschuang Dschou. Plötzlich wachte er auf: da war er wieder wirklich und wahrhaftig Dschuang Dschou. Nun weiß ich nicht, ob Dschuang Dschou geträumt hat, dass er ein Schmetterling sei, oder ob der Schmetterling geträumt hat, dass er Dschuang Dschou sei, obwohl doch zwischen Dschuang Dschou und dem Schmetterling sicher ein Unterschied ist. So ist es mit der Wandlung der Dinge.“ Dieser *Schmetterlingstraum* des daoistischen Klassikers Dschuang Dschou (Zhuangzi) sowie das auf die Erkenntnisse der Wahrscheinlichkeitstheorie zurückgehende und in der Literatur des 20. Jahrhunderts mehrfach thematisierte *Infinite-Monkey-Theorem* („Wenn eine unendliche Anzahl von Affen an einer unendlichen Anzahl von Schreibmaschinen zu spielen beginnt, wird schließlich einer von ihnen ein Theaterstück von Shakespeare schreiben“, so etwa der Science-Fiction-Autor Nevil Shute im Jahr 1957) bilden den Hintergrund, vor dem eine Geschichte sowie die mit der Geschichte zusammenhängenden Geschichten/Gerüchte, die in der Zeit um das Jahr 1960 für Aufsehen in der deutschsprachigen Literaturszene gesorgt haben, unter die Lupe genommen werden.

DAS TRANSHUMANISTISCHE KONZEPT VON DER SINGULARITÄT UND SEINE AUSWIRKUNG AUF DIE REORGANISATION DER MENSCHLICHEN ARBEIT IN WERKEN DER DEUTSCHSPRACHIGEN GEGENWARTSLITERATUR.

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Die künstliche Intelligenz hat eine immer stärkere thematische Präsenz in der deutschsprachigen Gegenwartsliteratur. Im Besonderen wird Kurzweils Konzept von der Singularität, dargelegt in seinem Buch „Die Intelligenz der Evolution. Wenn Menschen und Computer verschmelzen“ verfolgt. Es lautet, dass im Laufe der Evolution der technisch optimierte Mensch Teil eines allumfassenden Netztes sein wird, in dem das Bewusstsein des Individuums mit dem der anderen verschmilzt, demzufolge nur ein einziges Bewusstsein gibt, das für alle gemeinsam ist. Man weiß es dabei nicht, was das führende Element in ihm ist, ob es sich dabei um menschliche oder künstliche Intelligenz handelt, sowie ob durch die Technologien das menschliche Bewusstsein, dem der KI untergeordnet ist. In dieser Vision haben wir eine Gesellschaftsordnung, die alle bisherigen übertrifft. In einer Gesellschaft mit einem einheitlichem menschlich-maschinellm Bewusstsein haben die einzelnen Individuen keine Bedeutung. So eine Gesellschaft kann leicht globale wirtschaftliche und ökologische Probleme lösen, weil die Manipulation des gemeinsamen Bewusstseins außerordentlich leicht und effizient ist, und die Kontrolle über die ganze Menschheit in Realzeit erfolgt. Auf der anderen Seite trägt so eine Gesellschaft alle Züge eines totalitären Regimes, in dem die Diktatur auf eine sanfte, unmerkliche Art und Weise ausgeübt wird. Die Arbeitsverhältnisse werden dabei besonders betroffen und die menschliche Arbeit wird in solchen Gesellschaften neu definiert. Im Vortrag werden Beispiele aus etlichen Romanen wie Theresa Hannigs *Die Optimierer*, Marc-Uwe Klings *Qualityland*, Tom Hillenbrands *Hologrammatica* angeführt und neue Gesellschaftsentwürfe dargestellt.

DIE ROMANTISCHE SICHT AUF DEN MASCHINENMENSCHEN: E.T.A. HOFFMANN

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Hll. Kyril-und-Method-Universität zu Veliko Tarnovo (BG)

Deus ex Machina – die Götter der Ellada (Hephaestus) – Hexen und Dämonen im europäischen Mittelalter – ironische Nachdichtungen in der Moderne (Brecht): sie alle sind Transformationen einer Denkfigur, in der die Angst vor unüberwindbarer Krisis zugrunde liegt. In entsprechenden zeitgemäßen Figuren zeigt sich die Bemühung des Menschen, in ausweglosen Konfliktsituationen Hilfe von Grenzgängern zwischen Welten zu holen. Hier sei der Fokus auf die maschinengestützten Subjekte gerichtet. Sie sind interessant gerade mit ihrer hybriden Struktur – erfunden von Menschen, tragen sie Marker humaner Identität, die das Überschreiten der begrenzten Fähigkeiten ihrer Schöpfer ermöglichen und somit zur Verbesserung von Lebensqualität und Weltkonstruktion beitragen sollten.

Die Maschine als soziokulturelles und technologisches Phänomen hat mit der Konstruktion künstlicher Tiere angefangen, produktiv in diese Beziehung einzugreifen, bis sich der Mensch erdreistete auch Seinesgleiche zu erfinden. De Vaucansons 'verdauende Ente' (1738) demonstrierte Hauptfunktionen des Körpers. Von Kempelens Schachtürke (1769) sorgte weltweit für Furore. Obwohl Descartes lebensechtes Androidenmädchen Francine eher als Legende faszinierte, und der Schachtürke sich als Bluff erwies, ging die Vorstellung vom mechanischen Mitmenschen nie ganz verloren. Ein Vorstoß in diese Richtung geschah in der schöngeistigen Literatur als Kompensation der Tücken in der Realität mit deren Extrapolieren in der Phantasie. Am Übergang zur klassischen Moderne hat E. T. A. Hoffmann – ein Meister der romantischen Ironie, dieses modisch gewordene Thema angegangen.

Am auffälligsten zeigt sich das in seinem Kunstmärchen „Der Sandmann“ (1817). Die mechanische Puppe Olympia wird dem jungen Studenten Nathanael zum Verhängnis. Seine Verliebtheit verkehrt sich angesichts der Destruktion der Geliebten in Aggression, Wahnsinn und Todessehnsucht, um im Suizid das Ende der Konfliktsituation zu setzen. Im Kunstmärchen „Die Automaten“ (1814) erscheint eine Evolution des Schachtürken zum Wahrsager, der sich mit Menschen unterhält und den künftigen Lauf von Dingen und Schicksalen voraussagt. Die Intellektualisierung des Kunstmenschen verbindet sich mit der romantisierten Interpretation des Themas. Die Verteufelung des Weiblichen im „Sandmann“ weicht hier der Verklärung der unsichtbaren Musikanten zur himmlischen Harmonie. Die Engelsstimme der Geliebten erscheint vermittelt durch beide Freunde, und das Böse wird zwar

nicht verdrängt, aber in den versetzten Episoden einer nicht linearen Handlung aufgehoben, so dass sich die fiktive Welt als ephemere und vielleicht imaginär darstellt.

Die deutschen Romantiker haben einen besonderen Stellenwert in der europäischen Moderne. Ihre Ironie ist realitätsbezogen in der philosophischen wie auch psychoanalytischen Art. Die Reflexion der Menschenmaschine erscheint in der Belletristik als Kunstgriff zur Darstellung des epochalen Unbehagens an der Dialektik zwischen der geglaubten intellektuellen Macht des menschlichen Genius und der Skepsis gegenüber der Erkennbarkeit der Welt, der Sehnsucht nach der Ferne und dem Festhalten am Subjektivismus des Ichs für sich (Fichte).

**GEFAHREN DER ENTWICKLUNG KÜNSTLICHER INTELLIGENZ AM
BEISPIEL VON RAPHAELA EDELBAUERS ROMAN *DAVE* (2021), KAI-FU
LEES SAMMELBAND *KI 2041. ZEHN ZUKUNFTSVISIONEN* (2022),
MICHAEL STAUFFERS HÖRSPIEL *DAS GROSSARTIGE MIMEI* (2023) UND
AUSGEWÄHLTEN FILMISCHEN WERKEN DER GEGENWART**

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In „Die Antiquiertheit des Menschen“ warnt Günther Anders bereits am Anfang des 20. Jahrhunderts vor möglichen verheerenden Folgen des technologischen Fortschritts: „Wer heute durch die Maschinen gefährdet ist, ist ja nicht der Handwerker [...]; auch nicht nur der Fabrikarbeiter [...]; sondern jedermann; und zwar jedermann deshalb, weil jedermann effektiv Konsument, Verwender und virtuelles Opfer der Maschinen und Maschinenprodukte ist.“ [1] Ulrich Beck stellt in „Weltrisikogesellschaft“ die „Legitimierung neuer Technologien“ in Frage, die sich global durchsetzen und den Menschen in Abhängigkeit von industriellen Verfahren bringen: „Durch die Zukunftstechnologien – der Genetik, der Nanotechnologie und der Robotik – öffnen wir ‚eine neue Büchse der Pandora‘. Gerade deshalb dürfte es in Zukunft kaum mehr genügen, wenn die Verantwortlichen einer gut gemeinten Forschung und technologischen Entwicklung in der Öffentlichkeit den gesellschaftlichen Nutzen und das geringe ‚Restrisiko‘ ihres Vorhabens beteuern.“ [2].

In meinem Beitrag will ich den Nachweis für die These erbringen, dass sowohl die Gegenwartsliteratur als auch zeitgenössische Filmproduktionen die Rezipient:innen vor der Anwendung der künstlichen Intelligenz warnen. Diese These wird anhand ausgewählter literarischer und cineastischer Werke veranschaulicht. Eine erschreckende Vision, in der sich die Grenzen zwischen Realität und virtueller Welt verwischen, entwickelt Raphaela Edelbauer in „DAVE“ (2021). Dieses Science-Fiction-Szenario stattet eine künstliche Intelligenz mit menschlichem Bewusstsein aus. Dem Rechner unterlaufen jedoch Fehler, die weitere Defekte in der Software auslösen und bald auch das Leben von Romanprotagonist:innen gefährden. Im Sammelband „KI 2041: zehn Zukunftsvisionen“ (2022) präsentiert Kai-Fu Lee beängstigende Bilder einer Welt, die sich durch den Gebrauch der künstlichen Intelligenz verändert hat. So plant ein Münchner Professor der Quantenphysik KI-gesteuerte Waffen, die die Gesellschaft ins Chaos stürzen lassen. In Michael Stauffers „Das großartige Mimei“ (2023) befähigt ein Computerspiel namens

„Superknospe“ hingegen jeden Spieler, sein eigenes, individuelles Universum zu erschaffen: von der kleinsten Zelle bis hin zu neuer Zivilisation und Herrschaft über den Kosmos. Ein fiktives Presseinterview zeigt die imaginäre Gestalt des Schöpfergottes, den der frevelhafte Leichtsinns der Menschheit entsetzt, die sich anmaßt, in der Vereinzelung eine individuell angepasste Welt zu schaffen, die auf den Kontakt mit den Menschen verzichtet. Als Gegenmaßnahme entwirft der Herr das sog. Mimei, eine Art sprachfähige ovale Skulptur, die den Nutzenden einen attraktiven Begegnungsraum bietet, in dem sie fasziniert die Eiform bewundern und selbstsüchtige Pläne vergessen. Die den Text prägende Ironie verstärkt die Aussage des Hörspiels. Der Schweizer Autor ist überzeugt, dass die Menschheit dabei ist, sichere Grenzen der Wissenschaftsentwicklung zu überschreiten, was zur Vereinzelung und Vereinsamung des Individuums führen wird. Auch zahlreiche filmische Werke beschwören die Gefahren einer fortschreitenden Digitalisierung. In Spike Jonzes Hollywood-Produktion „Her“ (2013) verliebt sich ein einsamer Mann in die weibliche Computerstimme einer lern- und gefühlfähigen Software, was schlimme Folgen für die Zukunft der Menschheit befürchten lässt.

Die Angst vor der Technik als Kontrollinstanz unserer Existenz führt in der Gegenwartskunst zu immer erschreckenderen Szenarien, in denen Maschinen zunehmend Leib und Leben der Bürger:innen bedrohen. Im Geist des aufgeklärten Katastrophismus verweisen die genannten Autor:innen auf ihre Ablehnung der fortschreitenden Digitalisierung. So lassen sich ihre Werke nicht nur als spannende Thriller, sondern auch als Warnung vor einem kritiklosen Vertrauen in die technischen Entwicklungen lesen, auch als Ausdruck ihrer Bedenken in Bezug auf den Zustand unserer Zivilisation. Ausgehend von singulären Störfällen bzw. folgenreichen Ereignissen im Leben individueller Bürger:innen erweitert sich die Erzählperspektive hin zu globalen Bedrohungen.

References:

- [1]. Anders, Günther: „Die Antiquiertheit des Menschen“, Bd. I. „Über die Seele im Zeitalter der zweiten industriellen Revolution“. München: C. H. Beck 1956, S. 6.
- [2]. Beck, Ulrich: „Von der Antiquiertheit des linearen Fortschritts pessimismus“. In: Ulrich Beck: „Weltrisikogesellschaft“. 4. Auflage. Suhrkamp Verlag: Frankfurt am Main 2015 [2008], S. 38–39.

ZWISCHEN KOLLEKTIVER UND KÜNSTLICHER INTELLIGENZ. GRUPPENAKTEURE IN DER DEUTSCHSPRACHIGEN GEGENWARTSLITERATUR

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Mitten im öffentlichen und literarischen Diskurs über Identitätspolitik und Intersektionalität legt Sibylle Berg den Schwerpunkt ihrer Romane GRM. Brainfuck (2020) und RCE. #RemoteCodeExecution (2022) ausgerechnet auf das aktivistische und erzählerische Potenzial der Gruppe. Sie lässt nicht, wie zurzeit üblich (1), eine Einzelfigur als Ich-Erzähler:in ihre individuellen Diskriminierungserfahrungen und unterprivilegierte Genealogie rekonstruieren, sondern nimmt eine Gruppe Jugendlicher ins Visier, die im Großbritannien nach Brexit, in einer spätkapitalistischen Apokalypse aufwachsen. Oft als hoffnungslose Dystopien kritisiert, verfolgen Bergs rezentesten Romane ein antipsychologisches Programm. Schonungs- und emotionslos wird von den Figurenkollektiven berichtet, die sich in der Welt der digitalen Wirtschaft zurechtzufinden versuchen, dagegen rebellieren und sich schließlich daran anpassen müssen.

Der Vortrag soll Bergs Romane mittels der Kontrastfolie eines dominanten „Populären Realismus“ (2) als einer Reflexion über die Möglichkeiten des kollektiven Handelns und Erzählens charakterisieren. Anstatt Repräsentativität und kollektive Gültigkeit durch den Blick in die intergenerationelle Vergangenheit zu beanspruchen, verortet Berg die Handlung ihrer Romane in der nahen Zukunft und konfrontiert ihre Figuren nicht mit persönlichen Traumata, sondern mit den Tücken und der Perfidität von KI und anonymem Code, die über ihr Leben entscheiden.

Bergs Romane stehen in die Tradition der Nachkriegsliteratur einer Elfriede Jelinek, die durch ähnliche Erzählkonstellationen die Ausweglosigkeit der österreichischen Nachkriegsjugend in Texten wie *Michael* (1972) und *Die Ausgesperrten* (1980) darstellte. Vor diesem Hintergrund soll der Vortrag die Allianzen und Spannungen zwischen einer kollektiven und einer künstlichen Intelligenz aufdecken und nach den Verbindungen zwischen neuer Technologie und experimentellen Erzählformaten suchen.

References:

1. Moritz Baßler: Populärer Realismus. Vom International Style gegenwärtigen Erzählens, München 2022.
2. Baßler: Populärer Realismus

CONTRASTIVE LANGUAGE STUDIES, CORPUS TECHNOLOGY AND AI // SPRACHVERGLEICH, KORPUSTECHNOLOGIE UND KI

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The talk is made up of three topics that are related to each other in a very structured way. It will on the one hand show how fast ideas have outgrown these last years with respect to language technology supporting contrastive language analysis by resolving legal and methodological issues. We will firstly link our presentation to a project of 2016-2019, that is to be related to a Research group linkage programme of the Alexander von Humboldt-Foundation (Institutspartnerschaft Leibniz-Institut für Deutsche Sprache, Rumänische Akademie Institute für Computerwissenschaften in Bukarest und Iași und Universität Bukarest), namely DRuKoLA, placed at the beginning of contrastive corpus technology within the ongoing project EuReCo of the Leibniz-Institut für Deutsche Sprache in Mannheim. Therefore, we will present concepts and ideas beyond these two acronyms and about a new emergent way of contrasting language data by means of building virtual comparable corpora (cf. Cosma & Kupietz 2019).

On the other hand, as language technology develops, within the Institute for German Language closely connected to AI research since its foundation in 1964, it is a natural progression that, in addition to traditional, so-called count-based, also predictive language models, trained on vast language data sets that are increasingly growing within the German Reference Corpus DeReKo and the Reference Corpus of Contemporary Romanian Language CoRoLa, it will provide new ways of understanding language and investigating differences between languages. In this context, the LLMs serve as models of the vast language experience of a language community. In order to gain insights despite the size of the models comparable to GPT-3, model parameters are manipulated in a targeted manner, e.g. by hiding all language experiences except for those from one decade, and dimensions are reduced to make the most important effects of the manipulation and relations between words immediately visible. This can be considered to be cutting-edge research situated at the convergence of Corpus linguistics and AI, leading to a better understanding of the syntagmatic and semantic relations of words, and how it is influenced by context factors.

CHATGPT AND IMPLICATIONS FOR AUTHORSHIP: THE (IM)POSSIBLE CREATOR

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In the framework of a research project “The gravity of academic plagiarism in the perception of scholars, students, and science policy makers in Bulgaria”, funded by the National Scientific Fund, we have been exploring the subject that has been the preoccupation of scholars across disciplines, especially with the open access release of ChatGPT in November 2022, and the implications of its use for research.

In this contribution, we focus on the implications of using Large Language Models with their enhanced capabilities of generating convincing imitations of human natural language [1] for our conception of authorship. Contextualizing this capability to the realm of academic production, we seek to explore whether generative AI is going to further add to the postmodern idea of the “death of the author” [2], and how it relates to the notion of academic integrity in one of its most ostensible features – awarding credit for other scholars' ideas. The discussion is conducted in terms of its integration into our understanding of academic integrity, and, in particular, our understanding of plagiarism.

References

[1] Bender, E. M., Gebru, T., McMillan-Major, A., & Shmitchell, S. (2021, March). On the dangers of stochastic parrots: Can language models be too big??. In *Proceedings of the 2021 ACM conference on fairness, accountability, and transparency* (pp. 610-623).

[2] Barthes, R. (1977). *The Death of the Author* (1968) (Trans: S. Heath). In *Image Music Text* (pp. 142-148). Fontana Press.

WENN MASCHINEN SEHEN UND HÖREN LERNEN: ZUR AUDIOVISUELLEN TRANSFORMATION

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Im Zeitalter der Künstlichen Intelligenz (KI) vollzieht sich eine tiefgreifende Transformation durch die Fortschritte in der audiovisuellen Übersetzungstechnologie. Unsere Aufmerksamkeit richtet sich auf die Auswirkungen und Potenziale dieser Entwicklung, wobei der Schwerpunkt auf KI-Systemen liegt, die imstande sind, audiovisuelle Daten zu analysieren und zu verarbeiten. Das Vermögen dieser Systeme, visuelle und auditive Informationen zu interpretieren, birgt das Potenzial, Sprach- und Kulturbarrieren zu überwinden, die Kommunikation zu erleichtern und den Zugang zu globalen Inhalten zu erweitern. Durch die detaillierte Analyse der aktuellen technologischen Trends und praktischen Anwendungen, einschließlich unter anderem automatischer Spracherkennung (ASR), Sprache-zu-Text-Transkription (STT) und Text-zu-Sprache-Software (TTS) sowie neuronaler maschineller Übersetzung (NMT), werden die Herausforderungen und Chancen beleuchtet, die sich aus der Integration visueller und auditiver Daten in die KI-gestützte Übersetzung ergeben. Darüber hinaus wird erörtert, wie diese Entwicklungen die traditionellen Übersetzungsprozesse transformieren und welche ethischen sowie gesellschaftlichen Implikationen sie ermöglichen.

Keywords: audiovisuelle Übersetzung, künstliche Intelligenz, maschinelle Übersetzung

ARTIFICIAL INTELLIGENCE AND COMPOSITION OF MUSIC

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Musical composition is a generative process which can be regarded as structuring preconceived musical models. This notion is reflected in a whole system for teaching musical composition that was developed and taught to students for more than 200 years (1600s – early 1800) – the partimento. This presentation aims to connect the application of AI in mimicking the process of composition based on structure. The current neural network model of the research adapts a Variational autoencoder for training and generating musical pieces. It takes as input the MAESTRO midi corpus. The generated results show that the chosen neural network is capable of generating musical pieces that poses traits of musicality and musical structure. However, the network shows some limitations – especially in transitions between musical structures the results tend to be more chaotic than structured. This can be regarded as an ability of the neural network to differentiate between *fest* and *locker* musical structures.

PREVALENCE AND TISSUE COLOCALIZATION OF NEUROTROPIC VIRUSES IN NATURAL AND POTENTIAL RESERVOIR HOSTS IN NIGERIA

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The recent wave of pandemic/epidemics in the world has necessitated that Africa join the global push to not only be ready for future pandemics but to also preempt them. Africa is plagued with a lot of neglected tropical diseases, many of them caused by neurotropic viruses. With minimal funding of these diseases, the burden they create on quality of life and productivity of animals has not been well estimated. More important is the need for active surveillance of possible reservoir hosts for some of these Neglected Tropical Diseases, so as to properly understand their epidemiology.

The term 'Arbovirus' is used to describe viruses from various families (majorly Flaviviridae, Togaviridae, Bunyaviridae) which are transmitted by arthropod vectors. Some of the diseases caused by arboviruses including Yellow fever, Dengue fever, Crimean-Congo haemorrhagic fever, and diseases caused by West Nile, Zika, and equine encephalitis viruses are of global public health concern. The need for constant monitoring of known (endemic) and relatively unknown (emerging) arboviruses in West Africa is crucial due to increased animal trade and movement, bird migration, and global climatic change which greatly impact on occurrence of these diseases because of the effect on the life cycles of the transmitting vectors. Across West Africa, the true economic and public health impact of these diseases are scarcely studied, with consequent paucity of current information. Using the Humboldt Research Hub grant, we are building a Center of Excellence with the focus of detecting and identifying endemic and emerging arboviral threats in West Africa, in addition to responding to any viral threat as they emerge. In this presentation, I will be speaking on current and emerging threats of SARS-Cov2, West Nile, and Influenza viruses, and the roles that reservoirs may be playing for reverse zoonosis. I will highlight our efforts of tissue localization of the West Nile virus in reservoir hosts

ANTIVIRAL ACTIVITY OF PHOTSENSITIZERS AND MICROALGAE EXTRACTS AGAINST BOVINE CORONAVIRUS

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Coronaviruses (CoVs) belong to the group of enveloped positive-sense single-strand RNA viruses. Beta CoVs revealed a great potential to cross the barrier between species by causing three epidemics/pandemics among humans in the 21st century. Considering the urgent need for powerful antiviral agents for decontamination, prevention, and treatment of CoV infections, we turned our attention to possibilities for virus inactivation with photosensitizers or natural products. In the present study, we evaluated for the first time the antiviral activity of the photosensitizer toluidine blue O (TBO) and two dichloromethane extracts (MEs) obtained from the microalgae species *Tetrademus acutus* against Betacoronavirus 1 (BCoV). In a consequential procedure, we determined the in vitro cytotoxicity of TBO and both MEs on MDBK cells with ISO10993-5/Annex C. The titer of BCoV propagated in MDBK cells was measured with TCID₅₀ assay and digital droplet PCR (ddPCR). The antiviral activity of the test samples in non-toxic concentrations was estimated using the direct inactivation approach (BCoV MOI = 1). The in vitro cytotoxicity was calculated in the MAPLE[®] mathematical software with developed by us programs for non-linear modeling and response surface analysis. The median effective concentration of TBO was 0.005 µM (selectivity index 170). Both MEs protected the MDBK cells from the BCoV induced cytopathic effect in concentrations 0.15 – 0.25 mg/mL. The ddPCR analysis revealed decrease in the number of virus particles after TBO or MEs treatment. In conclusion, TBO and MEs exhibit significant potential for direct inactivation of BCoV in vitro and should be subjected to further investigation aiming at possible application in the veterinary and/or human medicinal praxis.

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PATHOLOGICAL FINDINGS IN RABBITS INFECTED WITH PSEUDOTYPED VIRUSES EXPRESSING THE SARS-COV-2 SPIKE PROTEIN

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Coronaviruses (CoVs) are RNA-viruses causing a broad spectrum of diseases in several species. The pandemic outbreak of COVID-19 has revealed their ability to jump from one host species to another thus becoming a global health problem, as far as the causative agent SARS-CoV-2 is a betacoronavirus and a new human pathogen. In light of the CoV zoonotic risk it appears pivotal to understand the pathogenesis and mechanisms of tissue injury of known CoVs within the “One-Health” concept. Aim of the current study was to develop a suitable BSLII animal model for investigation of coronavirus pathogenicity. For this purpose, easily traceable intracellularly synthetic VLPs/pseudocapsids expressing the Delta and Omicron type of the Spike protein were generated. New Zealand rabbits were injected intravenously with 10^6 virus particles. Blood samples, were collected at 1st, 7th, 14th and 21st days after infection. Some clinical, e.g. haematological and biochemical parameters were measured. Tissue samples from aorta, lung, and heart were subjected to pathomorphological analysis. Total protein lysates were prepared from the same samples and the expression of selected metalloproteases was evaluated. Changes in some haematological (leuco-, eritro- and thrombocytosis) and biochemical (glucose, total protein, enzymes AST, ALT, AMY, BUN) parameters were found depending on the time after infection and type of viral particles. Some changes in the pathomorphological structure of the examined viscera were observed. For the rabbit injected with the Δ virus particles the outcome of the infection was premature death at day 21. In conclusion, the preliminary results are promising and the experiments to establish a model for evaluation of SARS-CoV-2 pathogenesis continue further.

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BACTERIAL ISOLATES FROM BATS - POTENTIAL SOURCES OF ANTIMICROBIAL RESISTANCE?

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Bats (order Chiroptera), and their guano are associated, apart from viruses, with intestinal pathogenic bacteria. Enterobacterial strains often have an intrinsic antimicrobial resistance (AMR) and can transmit it to other bacteria of the same or different species through horizontal gene transfer. Multidrug resistant bacteria are present in bat guano worldwide, likely due to contact with antibiotic treatment waste. A pioneering study was performed, regarding the intestinal microbiota of Bulgarian bat species and its AMR profile. It included cultivation on selective media, the Kirby-Bauer disc diffusion method, matrix-assisted laser desorption/ionization-time of flight mass spectrometry, the automated system PhoenixTM M-50, PCR, etc. Diverse species were isolated from the greater horseshoe bat (*Rhinolophus ferrumequinum*), mainly from the order Enterobacterales: *Escherichia coli*, *Yersinia enterocolitica*, *Hafnia alvei*, *Citrobacter braakii*, *Proteus vulgaris*, *Providencia rettgeri*, *Morganella morganii*, etc. *Pseudomonas* strains and the Gram-positive *Enterococcus faecalis* were also found. The isolates include commensals in the animal and human gut, opportunistic pathogens and obligate pathogens, such as *Y. enterocolitica*. The current study is one of the rare cases documenting the presence of *Leptospira* sp. in fecal samples; its pathogenic potential was unknown. The intrinsic AMR of a few isolates to ampicillin, nitrofurantoin, colistin, etc. was confirmed. Ten strains were identified as potential producers of extended-spectrum beta-lactamases (ESBLs): *C. braakii*, *H. alvei*, etc. Fourteen strains were potential producers of inducible AmpC. Possible production of metallo- β -lactamases (MBLs) was confirmed in several strains. In *M. morganii*, *H. alvei*, *Enterobacter asburiae* and *Enterobacter cloacae*, the simultaneous production of ESBLs, AmpC and MBLs was confirmed. Atypical resistance to

some of the tested antibiotics was found, most likely acquired through contact with waste from antibiotic treatment of animals and humans, and/or transfer of AMR from humans and the environment to bats.

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WIDELY NEUTRALIZING ANTIBODIES TO CONSERVED VIRION STRUCTURES OF HIV – A NEW PERSPECTIVE FOR VACCINES TARGETING VIRUSES WITH HIGH MUTATION RATE

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Despite significant advances in antiretroviral therapy (ART) over the past forty years, developing an effective HIV vaccine remains essential for a sustainable solution to the HIV epidemic. This report reviews two promising approaches to creating a preventive HIV vaccine.

1. mRNA technology and creating antibodies

Current research emphasizes the development of broadly neutralizing antibodies (bNAbs) targeting seven highly conserved regions on the HIV envelope (Env) glycoprotein. This approach utilizes an mRNA platform incorporating multiclade Env-gag virus-like particles (VLPs). The mRNA vaccine delivers genetic instructions to produce fragments of the Env and Gag proteins, which assemble into VLPs. These VLPs are recognized by the immune system, prompting it to generate bNAbs capable of neutralizing multiple HIV strains. Studies in Rhesus macaques demonstrated a 79% risk reduction per exposure to HIV compared to non-vaccinated animals. Additionally, this vaccine induces a robust T-cell response, and combining it with anti-HIV antibodies has shown to suppress the virus for several months without daily ART.

2. Cell-based immune response

Another strategy focuses on eliciting a potent cell-based immune response using an immunogen created by inserting selected HIV genes into a cytomegalovirus (CMV) vector. CMV naturally persists at low levels in the body, maintaining a large T-cell response. Preliminary tests in monkeys infected with SIV (simian HIV) showed that vaccination with a CMV-based immunogen led to the complete elimination of SIV in the majority of animals. The CMV vector-based vaccine, VIR-1111, targets CMV-seropositive individuals. This weakened CMV vector has the potential to deliver and maintain HIV vaccine material for extended periods, possibly overcoming the issue of waning immunity seen with other vaccine vectors.

These innovative approaches hold promise for developing an effective HIV vaccine, offering new hope in the fight against this highly mutable virus.

BEWERTUNG DER WIRKSAMKEIT DES COVID-19-IMPfstOFFS IN EINEM LAND MIT GERINGER IMPFABDECKUNG: ERKENNTNISSE AUS REALEN DATEN UND PROPENSITY-SCORE-MATCHING-ANALYSEN

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Wir haben eine umfassende Bewertung der Wirksamkeit des COVID-19-Impfstoffs bei der Senkung der Sterblichkeitsraten in einem Land mit niedriger Impfrate durchgeführt. In einer retrospektiven Kohortenstudie wurden Daten von 1.048.574 erwachsenen (≥ 18) Patienten aus dem Zeitraum von März 2020 bis April 2022 analysiert, wobei Daten aus dem nationalen digitalen Patientendatenarchiv verwendet wurden. Mittels univariater Analyse und logistischer Regression wurden die Quotenverhältnisse und ihre Signifikanz berechnet. Zur Verstärkung der statistischen Ergebnisse wurde Propensity Score Matching verwendet. Von den 1.048.574 mit COVID-19 diagnostizierten Patienten waren 73 % ($n = 780.718$) ungeimpft und 27 % ($n = 267.856$) vollständig geimpft. Nicht adjustierte statistische Analysen zeigten eine signifikante Reduktion der Sterblichkeitsrate in der geimpften Kohorte (1.608 Todesfälle; 0,6 %) im Vergleich zur ungeimpften Gruppe (40.985 Todesfälle; 5,2 %) [OR 0,1090 (95 % KI 0,1037 bis 0,1146), $p < 0,0001$]. Dieses Ergebnis war über alle Untergruppen hinweg konsistent, einschließlich Patientengeschlecht, Altersgruppe, Krankenhausumgebung, Impfstofftyp, SARS-CoV-2-Variante und Hochrisikopatientengruppen (d. h. mit einer soliden malignen Erkrankung, Herz-Kreislauf-Erkrankung, chronischer Lungenerkrankung oder Diabetes mellitus). Die logistische Regression ergab, dass das höchste Sterberisiko bei nicht geimpften Männern über 63 Jahren besteht. Das Propensity-Score-Matching untermauerte die beobachtete Reduktion der Sterblichkeitsrate in der gesamten geimpften Kohorte und innerhalb aller Patientenuntergruppen. Personen, die mit SARS-CoV-2 infiziert sind, haben ein erhöhtes Risiko eines vorzeitigen Todes. Durch eine Impfung, insbesondere auf der Grundlage mRNA-basierter Plattformen, wird dieses Risiko insbesondere bei Hochrisikogruppen deutlich gemindert.

Schlüsselwörter: COVID 19; Impfung; Hochrisikopopulation; Mortalität;

CYTOTOXIC AND ANTIPROLIFERATIVE EFFECTS OF NEW POTENTIAL ANTIBACTERIAL AGENTS

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The honey bee (*Apis mellifera*) has been known to mankind since ancient times, but due to various causes including pesticides, bacterial diseases and parasites their populations have been declining dramatically worldwide [1]. That leads to a pressing problem with a huge global economic, environmental, social, and public health impact.

The American Foulbrood disease (AFB) is an infection that belongs to the most deleterious honey bee diseases [1,2]. Because of that we focused our work on investigating the cytotoxic potential of new small molecules against the Gram-positive bacterium *Paenibacillus larvae*, the causative agent of the American Foulbrood disease (AFB). Furthermore, we decided to study the activity of these compounds against different cancer cell lines.

As a result, three of the newly synthesized substances were found to possess an anti-bacterial activity against *P. larvae* and a strong cytotoxicity against all investigated tumor cell lines, including HepG2, MDA-MB-231, HT-29, and 3T3. The biological effects of these new compounds are comparable to those of the approved drugs lincomycin (an antibiotic) and doxorubicin (an antitumor agent). Based on their cytotoxic and antiproliferative activity two of the drug candidates were chosen for further studies identifying their mechanisms of action.

Acknowledgments:

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References:

[1] Ebeling, J. et al. *Appl. Microbiol. Biotechnol.* 2016, 100(17), 7387–95.

[2] Matović, K. et al. *Veterinary Sciences* 2023, 10(3), 180.

FROM IN SILICO TO IN VITRO EVALUATION OF NOVEL FACTOR XIIIa INHIBITORS

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Cardiovascular diseases (CVDs) remain a significant global health challenge, with high mortality rates attributed mainly to heart attacks and strokes. Anticoagulants inhibiting the activity of blood clotting factor XIIIa (FXIIIa), an enzyme involved in the last step of the coagulation cascade, reduce the stability and strength of the formed fibrin mesh and its resistance to fibrinolysis (the process of breaking down clots) [1]. FXIII is synthesized as two separate subunits (A and B) in different tissues, and these subunits assemble in the blood plasma to form an FXIII-A₂B₂ heterotetramer. After vascular injury the FXIII-A activation peptide is cleaved by thrombin and together with Ca²⁺-binding is activated to its active form – FXIIIa (FXIIIa₂). In this study, we present an innovative platform for structure-based drug design and screening relying on single crystal X-ray diffraction and molecular docking using the SeeSAR tool (SCXRD/SeeSAR) to analyse the interactions between the newly designed ligands (small molecules and peptidomimetics) and the active form of FXIIIa (PDB: 4KTY) [2] as well as its transitional states [3]. As a result, the binding affinities (including their physicochemical and drug-like properties) of selected small-molecular-based compounds using the embedded in SeeSAR “HYDE” (HYdrogen DEsolvation) algorithm were estimated. In addition, different substance classes FXIIIa inhibitors docked in orthosteric (catalytic site: Trp279, Gln313 and Cys314) and allosteric (around the catalytic site) binding sites are shown. The combination of computational modeling with experimental approaches advances our understanding of FXIIIa–inhibitor interactions and accelerates the drug design process of novel anticoagulants.

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Reference:

[1] Al-Horani, R.A. & Kar, S. *Eur. J. Med. Chem.* **2020**, 200, 112442.

[2] Stieler, M. et al. *Angew. Chem. Int. Ed. Engl.* **2013**, 52, 11930-11934.

[3] Schmitz, T. et al. *Anal. Biochem.* **2020**, 605, 113708.

COMPUTATIONAL STUDY TO PREDICT P-GLYCOPROTEIN BINDING POTENTIAL OF TYROSINE KINASE INHIBITORS FOR CANCER TREATMENT

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In silico methods have been proven a successful tool in drug discovery and design by utilizing big data and various modelling approaches to generate and optimize appropriate solutions. Among the most promising are the so-called structure-based methods that rely on known 3D structures of the drug targets, among them pharmacophore modelling, docking and virtual screening (VS). In this study we present a computational approach to identify tyrosine kinase inhibitors (TKIs) as binders of the multidrug resistance transporter P-glycoprotein (P-gp) for the purposes of improving anticancer drug efficacy by modulating P-gp mediated drug efflux. To identify TKIs that may act as putative P-gp binders a VS docking-based protocol was developed and validated. First, a training dataset (TKI-Pgp) was constructed by collecting structural and biological information for P-gp binding on 43 TKIs from the scientific literature and DrugBank. A second dataset for the VS purposes was created by extracting relevant structural data for 135 TKIs from ChEMBL (TKI-VS). A consensus pharmacophore model was derived by flexible alignments of the conformations of eight TKIs (a core set selected from the TKI-Pgp dataset) on the bioactive conformations of the well-known P-gp substrate Taxol and P-gp inhibitor Zosuquidar extracted from their 3D complexes with the transporter. Subsequent docking studies of the compounds from the TKI-VS dataset were performed in the human P-gp 3D structure without and with the derived pharmacophore as a filter. The VS outlined Fenerbrutinib (Phase 1 Bruton tyrosine kinase inhibitor) and Mobocertinib (FDA approved first-in-class EGFR_{exon20} inhibitor) as potential hits for P-gp binding. In conclusion, *in silico* approaches represent an indispensable strategy to identify lead structures in the design of Pgp modulators with the ability for restoring sensitivity to cytotoxic agents in resistant tumour cell lines.

THE CAROTID BODY: A POLYMODAL ARTERIAL CHEMORECEPTOR

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The carotid body (CB) is the main peripheral arterial chemoreceptor that plays an essential role in initiating respiratory and cardiovascular adjustments to maintain blood gas homeostasis. It is strategically located in the bifurcation region of each common carotid artery for monitoring blood chemicals just before they reach the brain, an organ that is critically sensitive to oxygen and glucose deprivation. This chemosensory organ consists of small clusters called glomeruli composed of two juxtaposed cell types, glomus and sustentacular cells, interspersed with blood vessels and nerve bundles, and separated by connective tissue. The neuron-like glomus cells contain numerous cytoplasmic organelles and dense-cored vesicles that store and release neurotransmitters upon stimulation. They are dually innervated by both sensory and autonomic nerve fibers. The glial-like sustentacular cells are regarded to be supporting cells although they sustain physiologic neurogenesis in the adult CB and are thus supposed to be progenitor cells as well. The CB is a highly vascularized organ and its intraorgan hemodynamics possibly plays a role in the process of chemoreception. Emerging evidence has shown that the CB is activated not only by hypoxia but also by other interactive stimuli, including hypercapnia, extracellular acidosis, hypoglycemia, and even by changes in physical parameters of the blood such as blood temperature and osmolality or reductions in blood flow, thus suggesting that it is a multimodal integrated metabolic sensor on purpose. It has also been revealed that the CB exhibits extraordinary structural and functional plasticity as a consequence of various environmental stimuli. Dysregulation of the CB function and altered oxygen saturation are implicated in various physiological and pathophysiological conditions, some of them highly prevalent in the human population. Therefore, expanding the knowledge on CB physiology and pathophysiology would increase our current understanding of respiratory homeostasis and cardiovascular responses in health and disease, while recent advances in human CB translational research would contribute to the development of promising novel targeted therapeutic strategies for sympathetic-related and cardiometabolic diseases. It can be inferred that the CB is a much more complex structure than hitherto thought, and at an organ-level it is comparable to a miniature brain.

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POTENTIAL ROLE OF AI IN DIAGNOSIS OF LOW TENSION GLAUCOMA

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Glaucoma represents a heterogeneous group of conditions with significant difference in pathogenesis, clinical characteristics, IOP levels, treatment approach and progression. It is a very complex disease without agreed upon diagnostic and classification criteria. Elevated intraocular pressure is main risk factor, and many treatment modalities are efficient for its reduction.

Very difficult diagnostic problem is caused by development of glaucomatous damage in patients that never had IOP above 21mmHg – so called Low Tension Glaucoma (LTG). The great value of Artificial Intelligence (AI) is the possibility to process and analyze multiple data from clinical exams and diagnostic testing. For onset and prognosis of LTG, systemic risk factors are more important. We hope AI to help in diagnostic definition for this dangerous glaucoma form, demonstrated in approximately 1/3 of patients.

We preformed retrospective clinical study of all LTG patients diagnosed and treated for 2 years period. Diagnosis was based on presence of glaucomatous nerve head damage, retinal nerve fiber layer (RNFL) thinning, characteristic visual field defects, and maximal intraocular pressure (IOP) < 21mmHg. Additionally, RR holter exam and Doppler echography were performed on selected patients, as well as consultations with cardiologist, neurologist and endocrinologist. Follow up period: 6-18 months. Disease progression was demonstrated in 65% of patients even after IOP decrease to 15-17mmHg. Most common findings were unstable blood pressure with nocturnal dips and IOP fluctuation.

Two metabolic phenotypes were observed. In the 1st group are patients in younger age who demonstrated signs of abnormal vasoregulation: Reynaud syndrome, migraine headache, systemic hypotension, cold hands and feet. Patients from 2nd group are older (around 80) with multiple systemic vascular problems, extreme fluctuations of RR and IOP, as well as cognitive problems.

The major concern is how to define LTG, and AI could help to reach unified diagnostic definition. We suggest for a need of new criteria for this glaucoma form – max IOP <15-18mmHg. Our studies support the vascular hypothesis for LTG development and progression. This glaucoma form is extremely challenging and mysterious, and both phenotypes group are mostly associated with ocular perfusion problems.

References:

- [1]. Fan N, Wang P, Tang L, Liu X (2015) Ocular Blood Flow and Normal tension Glaucoma. *Bio Med research International* Vol 2015, ID 308505
- [2]. Mariotoni EB, Datta S, Shigueoka LS, et al; Deep Learning-Assisted Detection of Glaucoma Progression in Spectral-Domain OCT; *Ophthalmol Glaucoma*. 2023 May-Jun;6(3):228-238
- [3]. AlRyalat SA, Singh P, Kalpathy-Cramer J, Kahook MY; Artificial Intelligence and Glaucoma: Going Back to Basics; *Clinical Ophthalmology* 2023;17 1525–1530
- [4]. Xiang Ji P, Ramalingam V, Balas M, et.al; Artificial Intelligence in Glaucoma: A New Landscape of Diagnosis and Management; *J. Clin. Transl. Ophthalmol*. 2024, 2(2), 47-63

ARTIFICIAL INTELLIGENCE IN THE FOLLOW-UP OF GLAUCOMA PATIENTS

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Introduction: Glaucoma is a potentially sight-threatening eye disease if not diagnosed and treated early. Artificial intelligence offers promising possibilities to improve the diagnosis and follow-up of glaucoma patients using data processing and image analysis algorithms.

Purpose: to present some capabilities of Artificial Intelligence in the processing and interpretation of examination data of glaucoma patients with potential for early detection of progression and correction in therapeutic approach.

Methods: literature research

Results: Some examples of the potential of artificial intelligence in the follow-up of glaucoma patients include, but are not limited to: the use of optical coherence tomography (OCT) data, computerized perimetry data, genetic testing, and personal data. OCT provides detailed images of ocular structures that are affected by glaucoma, such as the optic nerve and ganglion cell complex. Artificial intelligence can analyze these images to detect pathological changes and predict the progression of the disease. Perimetry test data are essential for assessing the visual field of glaucoma patients. Artificial intelligence can analyze this data to detect changes and track disease progression. Integration of genetic testing and personal data can help identify individual risks and personalize care for glaucoma patients. Artificial intelligence can process this data to predict the risk of developing the disease and determine the most appropriate prevention and treatment strategies.

Conclusion: The use of artificial intelligence could be of significant benefit to ophthalmologists and patients in the near future. This technology could help detect glaucoma disease earlier, personalize care, and improve therapeutic outcomes for patients.

INFLUENCE OF THE HOST GENOME ON COVID-19 SUSCEPTIBILITY AND SEVERITY OF DISEASE IN BULGARIAN PATIENTS

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Background/Objectives: Many efforts have been done to determine common genetic variants in the human genome contributing to the susceptibility, severity and outcome of COVID-19 infection. However rare pathogenic variants affecting host response to Sars-Cov-2 may also contribute to COVID-19 severity. Therefore, we aimed at searching for rare genetic variants in the human exome related to COVID-19 severity and outcome.

Methods: Whole exome sequencing (WES) was performed in 444 patients, admitted to hospital with confirmed SARS-CoV-2 infection, to search for associations between rare pathogenic/potentially pathogenic variants and COVID-19 severity. The gene panel analysed contained 1172 candidate genes previously reported in host genetic studies for COVID-19. The sample was divided depending on the severity (severe and critically ill, 41%; with moderate disease, 29%, and cases with mild or no symptoms, 30%). Comparisons were made between the groups. Statistical analysis was performed depending on the type of variables compared. STRING was used for protein -protein interaction network analysis.

Results: Altogether 519 rare pathogenic and likely pathogenic variants (PV/LPVs) were discovered in 244 genes and in 296 patients. We detected ultra-rare variants (MAF<0.01%) in immune response-related genes, already associated with the host response to COVID-19. No overall association with COVID-19 severity and outcome was found. However, in severely ill patients we detected known PV/LPVs in genes associated with diseases such as cardiovascular disease, cystic fibrosis, coagulation, primary immune disorder, DNA damage repair response, primary ciliary dyskinesia, etc. that might contribute to the severity of the illness. Additionally, we report 93 novel PV/LPVs in patients with severe disease. Among the affected genes are some of the well-established candidates for severe disease. A network analysis of the 244 genes containing PV/LPVs revealed a main component, consisting of 13 interconnected genes related to epithelial cilium to be statistically significantly association with severity.

Conclusions: Rare pathogenic variants might contribute to the severity and outcome of SARS-CoV-2 infection in at least a proportion of patients. Of particular interest are the PVs in genes involved in

the formation of cilia that might be associated with a more severe course and outcome in response to SARS-CoV-2 infection in the carriers.

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GERMLINE GENETIC ANALYSIS OF PATIENTS WITH ONCOLOGICAL DISEASES

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Hereditary factors play a key role in the risk of developing several cancers and identification of germline predisposition can have important implications. Hereditary cancer syndromes (HCSs) account for nearly 10% of cancers even though they are often underdiagnosed [1]. Most of HCSs exhibit an autosomal dominant inheritance pattern, with a 50% risk of transmission to offspring [2]. Example of such kind of HCSs are hereditary breast-ovarian cancer (HBOC), Lynch syndrome, Multiple endocrine neoplasia, neurofibromatosis type 1 and type 2, Li–Fraumeni syndrome, Familial adenomatous polyposis, Tuberous Sclerosis, *CHEK2*-associated hereditary cancer syndrome and others. There are also severe inborn disorders characterized by profound multiorgan failures, where cancer susceptibility constitutes only a part of clinical presentation of the disease (e.g., Bloom syndrome, Fanconi anemia, Nijmegen breakage syndrome, ataxia-telangiectasia, etc) and are due to biallelic inactivation of genes involved in DNA repair and are characterized by severe immune deficiency [3].

The population frequency of *BRCA1/2* mutations associated with HBOC and *MLH1/MSH2*-linked Lynch syndrome mutations are with high frequency approximately 1:300–1:400. This means that at least 2% of presumably healthy subjects carry germline pathogenic variants associated with highly increased risk for development of certain cancer types and these estimates can be significantly higher in populations with pronounced founder effect [3].

Germline genetic testing came to the forefront in the precision medicine era since it is with rising matter for risk assessment, screening and also treatment decisions for many oncological diseases. Variants detected in germline testing can be inherited by offspring and thus carrier testing for family members should be advised and this provides opportunity for genetically targeted primary disease prevention, early screening and risk reduction. It has been estimated in different studies that the overall pathogenic/likely pathogenic variants (PGV) prevalence in wide variety of cancer types is in the range of 3%-17.5% [4, 5, 6]. Using standard guidelines like National Comprehensive Cancer Network (NCCN), National Society of Genetic Counsellors (NSGC), American College of Medical

Genetics (ACMG), American Society of Clinical Oncology (ASCO) for selecting which patients to be tested and precise gene panels, 48% of patients with PGV would not have been detected. Based on the findings from germline genetic testing it was found that for nearly 30% of the patients with a high-penetrance PGV there was need for treatment modification. It should be taken into consideration the implementation of broad universal testing strategy instead of targeted strategy based on clinical guidelines for germline genetic testing of cancer patients [4].

Implementing germline genetic testing in clinical practice hides some challenges. One of these challenges is finding the most appropriate indication guideline choosing which patients to refer to genetic testing. Second it should be considered social, cultural, and religious barriers to genetic testing in some populations. There are challenges in variant interpretation and then with genetic counselling of patients according to the classification of the variant found (pathogenic, likely pathogenic and variant of unknown significance) and the penetrance of the gene (high, intermediate or low). There is need for interdisciplinary training of specialists to address genetic assessment, the interpretation of the results and implementation of genetic results for choosing treatment options. In patients with known PGV the decision regarding the extent and indication of surgery are also challenge. The decision is complicated because it depends not only on the mutational landscape but also depends on the patient age, education, family, culture, society and sometimes religious beliefs [7]. And the final challenge but not least is the high cost and availability of genetic testing.

In the presentation will be shown some results from germline genetic testing of patient with oncological diseases referred to Molecular Medicine Center as an example of the importance of genetic testing.

References:

[1] Jahn A, Rump A, Widmann TJ, Heining C, Horak P, Hutter B, Paramasivam N, Uhrig S, Geldon L, Drukewitz S, Kübler A, Bermudez M, Hackmann K, Pormann J, Wagner J, Arlt M, Franke M, Fischer J, Kowalzyk Z, William D, Weth V, Oster S, Fröhlich M, Hülleln J, Valle González C, Kreutzfeldt S, Mock A, Heilig CE, Lipka DB, Möhrmann L, Hanf D, Oleś M, Teleanu V, Allgäuer M, Ruhnke L, Kutz O, Knurr A, Laßmann A, Endris V, Neumann O, Penzel R, Beck K, Richter D, Winter U, Wolf S, Pfütze K, Geörg C, Meißburger B, Buchhalter I, Augustin M, Aulitzky WE, Hohenberger P, Kroiss M, Schirmacher P, Schlenk RF, Keilholz U, Klauschen F, Folprecht G, Bauer S, Siveke JT, Brandts CH, Kindler T, Boerries M, Illert AL, von Bubnoff N, Jost PJ, Metzeler KH, Bitzer M, Schulze-Osthoff K, von Kalle C, Brors B, Stenzinger A, Weichert W, Hübschmann D, Fröhling S, Glimm H, Schröck E, Klink B. Comprehensive cancer predisposition testing within the prospective MASTER trial identifies hereditary cancer patients and supports treatment decisions for rare cancers. *Ann Oncol.* 2022 Nov;33(11):1186-1199. doi: 10.1016/j.annonc.2022.07.008. Epub 2022 Aug 18. PMID: 35988656

[2] Garutti M, Foffano L, Mazzeo R, Michelotti A, Da Ros L, Viel A, Miolo G, Zambelli A, Puglisi F. Hereditary Cancer Syndromes: A Comprehensive Review with a Visual Tool. *Genes*

- (Basel). 2023 Apr 30;14(5):1025. doi: 10.3390/genes14051025. PMID: 37239385; PMCID: PMC10218093
- [3] Imyanitov EN, Kuligina ES, Sokolenko AP, Suspitsin EN, Yanus GA, Iyevleva AG, Ivantsov AO, Aleksakhina SN. Hereditary cancer syndromes. *World J Clin Oncol*. 2023 Feb 24;14(2):40-68. doi: 10.5306/wjco.v14.i2.40. PMID: 36908677; PMCID: PMC9993141.
- [4] Samadder NJ, Riegert-Johnson D, Boardman L, Rhodes D, Wick M, Okuno S, Kunze KL, Golafshar M, Uson PLS Jr, Mountjoy L, Ertz-Archambault N, Patel N, Rodriguez EA, Lizaola-Mayo B, Lehrer M, Thorpe CS, Yu NY, Esplin ED, Nussbaum RL, Sharp RR, Azevedo C, Klint M, Hager M, Macklin-Mantia S, Bryce AH, Bekaii-Saab TS, Sekulic A, Stewart AK. Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome. *JAMA Oncol*. 2021 Feb 1;7(2):230-237. doi: 10.1001/jamaoncol.2020.6252. Erratum in: *JAMA Oncol*. 2021 Feb 1;7(2):312. doi: 10.1001/jamaoncol.2020.7373. PMID: 33126242; PMCID: PMC7600058.
- [5] Mandelker D, Zhang L, Kemel Y, Stadler ZK, Joseph V, Zehir A, Pradhan N, Arnold A, Walsh MF, Li Y, Balakrishnan AR, Syed A, Prasad M, Nafa K, Carlo MI, Cadoo KA, Sheehan M, Fleischut MH, Salo-Mullen E, Trotter M, Lipkin SM, Lincoln A, Mukherjee S, Ravichandran V, Cambria R, Galle J, Abida W, Arcila ME, Benayed R, Shah R, Yu K, Bajorin DF, Coleman JA, Leach SD, Lowery MA, Garcia-Aguilar J, Kantoff PW, Sawyers CL, Dickler MN, Saltz L, Motzer RJ, O'Reilly EM, Scher HI, Baselga J, Klimstra DS, Solit DB, Hyman DM, Berger MF, Ladanyi M, Robson ME, Offit K. Mutation Detection in Patients With Advanced Cancer by Universal Sequencing of Cancer-Related Genes in Tumor and Normal DNA vs Guideline-Based Germline Testing. *JAMA*. 2017 Sep 5;318(9):825-835. doi: 10.1001/jama.2017.11137. Erratum in: *JAMA*. 2018 Dec 11;320(22):2381. doi: 10.1001/jama.2018.17511. PMID: 28873162; PMCID: PMC5611881
- [6] Rosenthal ET, Bernhisel R, Brown K, Kidd J, Manley S. Clinical testing with a panel of 25 genes associated with increased cancer risk results in a significant increase in clinically significant findings across a broad range of cancer histories. *Cancer Genet*. 2017 Dec;218-219:58-68. doi: 10.1016/j.cancergen.2017.09.003. Epub 2017 Sep 25. PMID: 29153097.
- [7] Al-Sukhun S, Masannat Y, Wegman-Ostrosky T, Shrikhande SV, Manirakiza A, Fadelu T, Rebbeck TR. Germline Testing Around the Globe: Challenges in Different Practice Settings. *Am Soc Clin Oncol Educ Book*. 2023 May;43:e390522. doi: 10.1200/EDBK_390522. PMID: 37220318.

ROLE OF HERPESVIRIDAE FAMILY IN PROSTATE CANCER ONSET, IMMUNOCOMPROMISED STATUS AND PROGRESSION IN THE TUMOR ENVIRONMENT

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Background: We aim to investigate the role of *Herpesviridae* family (*HHV*) in the onset and progression of prostate cancer (PCa). A local PCa immunological status profiling was made. **Material and methods:** In total 49 Bulgarian PCa patients with FFPE were analyzed. DNA/RNA extraction, Real-Time qPCR, and histological examination were applied. **Results:** Active infection with *EBV*, *CMV*, *HSV2*, *HHV6*, *HHV7* and *VZV* was detected in 69,4% of the PCa patients as follow 47%, 38%, 41% 2,9%, 2,9% and 5,8 % in contrast with significantly lower frequency (6 %) in the noninvasive controls. In *HHVs* infected FFPE the histo-pathological landscape includes: intratumor lymphocyte infiltration with fibrosis and necrosis, periductal chronic inflammatory reaction, granulomatous lesions with foci of abscesses and necrosis, inflammatory infiltration, chronic lymphadenitis, PIA, HGPIN, etc. The majority of viral infected PCa patients were determined as poorly and moderately differentiated /G3, G4 and G5/ prostatic tumors with features for aggressiveness, poor prognosis and progression: perineural, perivascular, lymphovascular invasion, seminal vesicle invasion, senile vesicle amyloidosis, lymph node metastasis, etc. In a small proportion of well-differentiated infected FFPE, a massive inflammatory process and foci of *HGPIN* were present, in contrast to uninfected ones without inflammation and tumor invasion. Investigated expression profile of *IL1 β* , *IL10*, *IL18*, *TNF- α* , *TLR4*, *GATA3*, *CD68* in PCa patients, infected with *HHVs* showed typical fluctuations associating with inflammatory inducible immunocompromised local status and prostate tumor progression.

Conclusions: *HHVs* are active in all clinical stages such as a long-term infection probably contributes for immunocompromised PCa profile. Persistent *HHVs* infection should be considered as a predictor for PCa progressive and unfavorable clinical scenario. Supported by the Grant D-299/18.12.2023; D-149/03.08.2023 of the MU-Sofia, Bulgaria

CHEMICAL FATE OF PHARMACEUTICALS IN THE ENVIRONMENT: NMR AND QUANTUM-CHEMICAL STUDY

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Pollution of the environment by drugs, their metabolites and degradation products is a hot environmental and public health topic [1]. The term "pharmacology" includes the knowledge of the chemical transformations of the drug induced by environmental conditions and the determination of the ecotoxicological properties of the degradation products. Among the factors that determine the chemical fate of a drug, water chlorination and the sunlight irradiation are of special importance. We use advanced spectroscopic techniques (NMR/EPR) for in situ monitoring of chemical reactions, preparative tools (LC-MS) for product isolation, and ecotoxicological assays on test organisms using standardized and accredited methods. The experimental part of the research is supported by the use of computational techniques (ab initio, DFT theoretical levels) that enable prediction and interpretation of the measured data [2].

The selection of a small library of drugs (eg. gemfibrozil, metformin or fluorouracil) is based on the pillars defining priority candidates for the 4th Watch List, which is in accordance with the Water Framework Directive. [3] Our research into the chemical and ecological profile of drugs includes an interdisciplinary approach and methodological synergy. This integration of different approaches can serve other researchers as an orientation for the redesign or implementation of new concepts for testing the chemical fate of drugs in the environment. The results on the chemical fate of the selected candidates provide a contribution to the constant effort of authority institutions to supplement official databases with missing information.

References:

- [1]. Ortúzar, M.; Maranda, E.; Rafael, O.-H.D.; Jesús, G.-L.; Elisabet, A. Pharmaceutical Pollution in Aquatic Environments: A Concise Review of Environmental Impacts and Bioremediation Systems, *Front. Microbiol.* 2022, 13:869332.
- [2]. Hok, L.; Ulm, L.; Tandarić, T.; Krivohlavek, A.; Šakić, D.; Vrček, V. Chlorination of 5-fluorouracil: Reaction mechanism and ecotoxicity assessment of chlorinated products. *Chemosphere*, 2018, 207,18:612.
- [3]. Gomez, L.; Marinov, D.; Sanseverino, I.; Navarro Cuenca, A.; Niegowska Conforti, M.; Porcel Rodriguez, E.; Stefanelli, F.; Lettieri, T. Selection of substances for the 4th Watch List under the Water Framework Directive, Publications Office of the European Union, Luxembourg, 2022.

SYNTHESIS, SPECTRAL STUDY, AND BIOLOGICAL ACTIVITY OF A NEW STYRYL QUINOLINIUM DYE

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Inflammation is a common symptom of many chronic diseases [1]. Anti-inflammatory drugs are accompanied by a large number of side effects. [2]. Due to the novelty of the study and limited information on the anti-inflammatory activity of styryl dyes, we tested a new styryl quinolinium dye. According to the World Health Organization (WHO), about a quarter of a million deaths per year are due to gastrointestinal diseases that are caused by various bacterial pathogens [3]. Some of the most commonly used antimicrobial compounds contain a quaternary nitrogen atom. The antimicrobial properties of styryl quinolinium dyes have been proven. The key structural fragment associated with the activity of these compounds is suggested to be the positively charged quinolinium cores [4].

A new styryl quinolinium dye was synthesized. The compound composition was confirmed by ¹H- and ¹³C NMR and IR-spectroscopy. Some physicochemical, pharmacokinetic, and the ADME profile were determined by *in silico* methods. The anti-inflammatory potential of the styrylquinolinium salt has been established *in vitro* and can be said to show promising activity. *In vitro*, the antibacterial activity of the dye was established against five strains of gram-positive bacteria, against three gram-negative bacteria strains, yeast, and fungi. Styrylquinolinium dye has the potential to be applied as a broad-spectrum antimicrobial agent.

References:

1. N.T. Ashley, Z.M. Weil, R.J. Nelson, Annual Review of Ecology, *Evolution, and Systematics* 43, **2012**, 385-406.
2. Y. Mizushima, M. Kobayashi, *Journal of Pharmacy and Pharmacology* 20, **1968**, 169-173.
3. World Health Organization, Appia, Geneva, Switzerland, **2015**, 1.
4. K. Chanawanno, S. Chantraprommaa, T. Anantapong, A. Kanjana-Opas, H. Fun, *European Journal of Medicinal Chemistry* 45 (9), **2010**, 4199-4208.

ABIOTIC METAL CATIONS IN MEDICINE: COMPUTATIONAL INSIGHTS INTO THE MECHANISM OF THEIR THERAPEUTIC ACTION

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Over the course of 3–4 billion years of organism evolution, several metal species of different oxidation states known as “native”, or “biogenic” have been chosen to participate in key biological processes as co-factors. On the other hand, there exist metals in nature outlined as “abiogenic species” with no known function in the body, which nonetheless exert a curative effect on the host organism. Such are silver (Ag^+), and gallium (Ga^{3+}) believed to be able to compete with the native cuprous (Cu^+), and ferric (Fe^{3+}) cations, respectively for binding some important proteins. Recently, we set on a quest for deciphering the most acclaimed mechanisms of therapeutic action of the aforementioned metal cations at atomic level by applying the powerful tools of computational chemistry.^{1–3} The obtained results shed light on the intimate mechanisms of metal recognition, thus revealing key factors governing the processes of native/abiogenic metal competition. This approach serves not only for explaining already existing experimental findings, but also as a first step in designing/engineering novel drug molecules of potential therapeutic value.

- (1) Kircheva, N.; Angelova, S.; Dobrev, S.; Petkova, V.; Nikolova, V.; Dudev, T. Cu^+/Ag^+ Competition in Type I Copper Proteins (T1Cu). *Biomolecules* **2023**, *13*, 681–694.
- (2) Kircheva, N.; Dudev, T. Gallium as an Antibacterial Agent: A DFT/SMD Study of the $\text{Ga}^{3+}/\text{Fe}^{3+}$ Competition for Binding Bacterial Siderophores. *Inorg. Chem.* **2020**, *59*, 6242–6254.
- (3) Kircheva, N.; Dobrev, S.; Petkova, V.; Yocheva, L.; Angelova, S.; Dudev, T. In Silico Analysis of the $\text{Ga}^{3+}/\text{Fe}^{3+}$ Competition for Binding the Iron-Scavenging Siderophores of *P.aeruginosa* - Implementation of Three Gallium-Based Complexes in the “Trojan Horse” Antibacterial Strategy. *Biomolecules* **2024**, *14*, 487.

EXPERIMENTAL STUDY OF SOME THERMODYNAMIC CHARACTERISTICS OF TWO- AND THREE-COMPONENT AQUEOUS SOLUTIONS OF STRONG ELECTROLYTES AS FUNCTIONS OF THEIR CONCENTRATION

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The present project combines theoretical modelling of important thermodynamic characteristics of aqueous solutions of strong electrolytes and conduction of laboratory experiments, which aim to validate the hypothesis put forward. The main focus of the work is to study the dependence of the boiling point of a solution T_b on its molar concentration c . Two independent theoretical models were proposed to describe the correlation - a linear and a non-linear one. Both of them were validated against relevant experimental data and as well compared with each other. For the numerical computation of the non-linear model an original ad hoc created computer script was used in the environment **MATLAB**. Theoretical values for the dissociation rate $\alpha(c)$ and the effective van 't Hoff factor's value $i_{\text{eff}}(c)$ for the used electrolytes have been computed and compared with the experiment. The results are summarized in tables and portrayed graphically, with an assessment of the accuracy.

References:

- [1] Andrews, F. C. Colligative Properties of Simple Solutions Science, 194(4265), 567–571, 1976
- [2] N. Saxena , D. K. Singh and M. M. Hussain Estimation of Molai Ebullioscopic Constants of Non-associated Solvents from Boiling Point Data Chemie, Leipzig, 268(1987), 392-394, 1984
- [3] McDonald J. E. Erroneous cloud-physics applications of Raoult's law Journal of meteorology, 1952
- [4] A. Wipf Thermodynamik und Statistische Physik, Theoretisch-Physikalisches-Institut Friedrich-Schiller-Universität, Jena, 69-71, 2018
- [5] Burt H. Car Roll, G. K. Rollefson AND J. Howard Mathews Ebullioscopic measurements in mixed solvents, J. Am. Chem. Soc, Vol.47, 1791 - 1799, 1926
- [6] P. G. Udyma Chemical and Petroleum Engineering, Plenum Publishing Corporation, Vol.3, 339-347, 1997
- [7] Holm H. Pauschmann 4 th International Conference on Separating Methods, With Special Reference to Chromatography, Journal of gaschromatography, Organic Chemistry Laboratory, Tbingen University, Tbingen, Germany Vol.6, 321 - 325, 1968

- [8] G. Cocco, C. Dejak and O. Devoto High precision and accuracy ebullioscopic measurements for a closer structural examination of concentrated solutions of strong electrolytes., *Chemical Physics Letter* Vol.11, 198 - 202, 1971
- [9] Brodale, G., Giaque, W. F. The Heat of Hydration of Sodium Sulfate. Low Temperature Heat Capacity and Entropy of Sodium Sulfate Decahydrate, *Journal of the American Chemical Society*, 80(9), 2042–2044, doi:10.1021/ja01542a003
- [10] C. Shin, C. M. Criss Standard enthalpies of formation of anhydrous and aqueous magnesium chloride at 298.15 K, Department of Chemistry, University of Miami, 1978
- [11] H. Jahn, G. Wolf Department of Chemistry, University of Miami, *Journal of Solution Chemistry*, Plenum Publishing Corporation, Vol. 22, 1993
- [12] G. Brodale, W. F. Giaque *J. Am. Chem. Soc.*, RY, Department of chemistry and chemical engineering, University of California, Berkley, Vol. 80, 2042-2044, 1957

ENZYMATIC BROWNING OR WHY FRUITS AND VEGETABLES LOSS THEIR QUALITY AFTER DAMAGING OF CELL INTEGRITY

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Enzymatic browning is an oxidative process that occurs in fruits and vegetables, when integrity of their cell structures is disturbed. It is due to enzymes (*phenolases*), which oxidize their substrates (*phenols*) into quinones in the presence of oxygen. Quinones polymerize and form a brown pigment called melanin. It results in undesirable food quality changes — in color, taste and texture [1]. Browning is a large problem for food industry and long-term storage of fruits and vegetables. It causes huge economic losses. The ways to control enzymatic browning have a practical meaning, making the topic hot [2].

The aim of the present study is to investigate the browning process in fruits and vegetables. Different species (apple, banana, banana peel, potato, mushroom) and various model systems (cut fruits; puree, juice, cell extract) were tested. The *Browning Index (BI)* of the samples was calculated using *Image J* program. *Absorbance spectroscopy at $\lambda=420\text{ nm}$* was used for phenolase activity assessment. The present results show that fruits and vegetables differ in their browning intensity and phenolase activity. The highest enzyme activity was discovered in banana/mushroom and the lowest one – in apple. An inhibitory effect of 1) *citric/ascorbic acids* and 2) *heating* on oxidative enzymes activity was also found. We observed that citric acid is less effective than ascorbic acid in suppressing phenolases. The highest enzymes thermostability was observed in banana (65°C). The phenolases in mushroom/potato keep their activity at 40°C, but are not stable at 65°C. Apple phenolases were unstable even at 40°C.

References:

- [1] Murata M: Food chemistry and biochemistry of enzymatic browning; *Food Science and Technology Research*, 28 (1), 1–12 (2022);
- [2] Moon K, Kwon E, Lee B and Kim C: Recent Trends in Controlling the Enzymatic Browning of Fruit and Vegetable Products; *Molecules*, 25(12): 2754 (2020).

TEXT AS SENSE, ILLUSION, AND THE BOOK OF CULTURE

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„Text“ is not an element of the lingual system system, but a format of communication which performs „sense“. Sense is realized as soon as a recipient knows the intention which motivates an utterance within a given context, usability decides if a text still is topical or, on the contrary, outdated. The definition of „text“ can only be achieved by a description of functions in regard to the recipient's expectation about the mode of reception [1] and about the use which can be made of the text. According to these criteria „text“ can be defined as „Knowledge storage in the form of a linearly-perspectivised action or re-enactment of argumentation, for the purpose of either a factual description of extra-linguistic circumstances (factual text) or for the purpose of empathic re-experiencing of extra-linguistic circumstances (aesthetic text)“ [2]. Finally, we are confronted today with texts generated not by human beings. Texts generated by AI do not pose a problem as long as their sense and applicability is known to the recipient. E.g. in telecommunications we perform flawlessly automated conversations, i.e. poly-auctorial oral texts, with answering machines, which may ask for personal credentials and the goal of our call before actually connecting us with a human fellow in the call centre. Likewise in written mediality, nobody feels unsure of oneself if confronted with operating instructions composed by a (translation) machine as long as the text's signifiers can be successfully applied to the signified (let's say your new DVD-player). But as soon as aesthetic texts are concerned we feel an 'inhumanity' of AI generated texts by supposing a lack of intentional communication. Our paper firstly will show by examples from (medieval) texts that the suspicion had always been ubiquitous, that a textual communicate only would simulating „sense“ but in fact is a compilation of signs without intention. Secondly, we ask if our findings may have importance regarding disputes about AI generated texts.

References:

- [1.] Eriksen, Stefka G. (2013): Mode of Reception and Function of Medieval Texts: A Comparative Study of Elye de Saint- Gilles and Elis saga ok Rósamundu. // *The Journal of English and Germanic Philology* 112/ 1, 1-25.
- [2.] Daiber, Thomas (2022): Texts become obsolete [Translated from German by Francis Michael Igrave]. // Gawrich, Andrea et al. (ed.): *Analysing Conflict Settings. Case studies from Eastern Europe with a focus on Ukraine*. Wiesbaden, 155-179: 166.

"EINE INTELLEKTUELLE HELDENTAT DES 9. JAHRHUNDERTS: KONSTANTIN VON PRESLAV UND SEIN LEHREVANGELIUM"

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Am Ende des 9. Jh. verfasste Konstantin, Bischof von Preslav sein bemerkenswertes Lehrevangelium. Es ist nicht nur ein Phänomen in der frühen kirchlichen Literatur Bulgariens, sondern hat auch eine Relevanz für die Geschichte der byzantinischen Literaturform der Katenen. Das Lehrevangelium ist die erste altbulgarische Predigtsammlung und trotz seines Kompilations- und größtenteils Übersetzungs-Charakters ein vollständiges Originalwerk, das in Bezug auf Konzeption, Kompositionsweise und literarische Form zum Zeitpunkt seines Erscheinens kein Vorbild in der byzantinischen Literatur hatte.

Es entstand als Erwiderung auf die Bedürfnisse der jungen bulgarischen Kirche und die Wichtigkeit einer raschen Christianisierung der slavischen Mehrheitsbevölkerung. Es beleuchtet und erklärt die Evangelien-Lesungen für alle Sonntagsliturgien nach dem beweglichen Kirchenkalender.

Die Sammlung umfasst 51 Predigten, die aus einer Einleitung, einem exegetischen Teil und einem paränetischen Schlusswort bestehen. Alle mittleren Teile stellen Übersetzungen von patristischen Kommentaren dar. Die Einleitungen und die Schlussworte, in denen der Preslaver Gelehrte seine eigene kirchliche und gesellschaftliche Lehre entfaltet, sind weitgehend eigenständige Texte. Gerade diese Teile machen die Einzigartigkeit der Predigten aus, indem sie sie zu besonderen kleinen Homilien formen.

Das ganze Vorhaben des Lehrevangeliums stellt Konstantin vor eine große intellektuelle Herausforderung und ist gleichzeitig ein Beweis für sein didaktisches und literarisches Können. Er klärt auf, indem er nicht nur aus dem Griechischen in die slavische Sprache übersetzt, die bis vor kurzem nie zum Verfassen literarischer, philosophischer und geistlicher Texte benutzt wurde, sondern auch die wichtigsten christlichen Dogmen und Postulate für die angehende Priester und die Neubekehrten in den Schlussworten nochmal verständlich auslegt. Aber er muss auch inspirieren, emotional berühren, überzeugen. Konstantin leistet höchstanspruchsvollste literarische, philologische und aufklärerische Arbeit, denn er versteht seine missionarische Aufgabe als Bestimmung seines Lebens und widmet ihr all seine geistlichen und intellektuellen Kräfte.

FROM PARCHMENT TO PROGRAMMING: AI'S ADVENTURES IN LANGUAGE ANALYSIS

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In recent years, we have witnessed rapid progress in the area of the digital humanities in general and Natural Language Processing (NLP) in particular. AI-based approaches have boosted the accuracy of tasks such as part-of-speech and full morphology tagging or lemmatization; Handwritten Text Recognition (HTR) tools have revolutionized the way we deal with manuscripts, thus paving the way for the efficient mass digitization of humankind's cultural heritage and the era of big(gish) data in the humanities disciplines concerned with historical documents.

In my paper, I report on current developments in this area, focusing on pre-modern Slavic, i.e. (Old) Church Slavonic or, in some contexts, Old (or Middle) Bulgarian. These low-resource language varieties, mostly written in the Old Cyrillic script, have a complex grammar and a high level of variation across the diachronic and diatopic dimensions, making it particularly challenging for NLP and other AI methods. I elaborate on the specific problems that arise due to the high variation of pre-modern Slavic and present and discuss results for different steps of the research cycle: specific and generic HTR models trained with different engines [1], post-correction with specialized tools and Large Language Models, part-of-speech and full-morphology tagging [2], lemmatization, classification [3], and working with uncorrected textual data [4]. I conclude my contribution with the presentation of selected real-world examples, demonstrating that old manuscripts and new technologies can be effectively combined to advance our understanding of historical texts.

References:

- [1]. Rabus, A.; Thompson, W. R. 2023. Performance of Generic HTR Models on Historical Cyrillic and Glagolitic: Comparison of Engines. *Scripta & e-Scripta* 23, 11–34.
- [2] Scherrer, Y., Mocken, S., Rabus, A. 2018. New developments in tagging pre-modern Orthodox Slavic texts. *Scripta & e-Scripta* 18, 9–33.
- [3]. Lendvai, P., van Gompel, M., Jouravel, A., Renje, E., Reichel, U., Rabus, A., Arnold, E. 2024. A Workflow for HTR-Postprocessing, Labeling and Classifying Diachronic and Regional Variation in Pre-Modern Slavic Texts. In: *Proceedings of Joint International Conference on Computational Linguistics, Language Resources and Evaluation (LREC-COLING 2024)*, May 2024, Torino, Italy.
- [4]. Rabus, A. 2024. Tolerating Imperfection: Uncorrected Transkribus Transcriptions in Church Slavonic Studies. In: Taseva, L.; Rabus, A.; Petrov, I. P. 2024. *Učitelno evanġelie na Konstantin Preslavski i juġnoslavjanskite prevodi na homiletični tekstove (IX-XIII v.)*. *Filologiġeski i interdisciplinarni rakursi*. Sofija, 453–467.

DIGITALINSTRUMENTE UND ALTSLAWISTIK: METHODOLOGISCHE BEMERKUNGEN

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Die Digitalisierung der Humanitaristik hat zweifellos neue Forschungsmöglichkeiten eröffnet. Die neuen Instrumente erlauben eine Beschleunigung und/oder Steigerung der Effizienz des Forschungsprozesses. Im Folgenden werden einige dieser Möglichkeiten hinsichtlich der methodologischen Fragestellungen kommentiert, die bei ihrer Anwendung zuerst adressiert werden sollten. In diesem Kontext seien als Beispiele die Vorbereitung der kritischen Ausgabe des Lebens Pachomius des Großen sowie die vorläufigen Arbeiten zu den Werken Isaak des Syrers in mittelalterlichen südslawischen Übersetzungen genannt.

USING ARTIFICIAL INTELLIGENCE TO STUDY INTELLECTUAL WORKS OF THE MIDDLE AGES – THE EXAMPLE OF THE MIDDLE BULGARIAN DIOPTRA TRANSLATION

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Using large collections of texts to answer research questions is a common method in many fields. Such corpora are especially useful for linguistic analysis if they contain linguistic metadata, i.e. lemmatization, morphological and syntactic annotation. It goes without saying that for large quantities of text such metadata cannot be provided manually. Automatic tools, such as modern neuronal taggers, are needed instead. However, working with historical language varieties, one might run into the problem that there is simply no data available with which these taggers could be trained. This is the case for the Middle Bulgarian.

By using data from similar language varieties, like Old Church Slavonic (Eckhoff et al. 2018) and Old East Slavic (Eckhoff/Berdičevskis 2015), and slightly adapting them, I was able to build a model that is successfully used in the annotation of the Middle Bulgarian *Dioptra* translation (Maion 2022). The bilingual edition of this poem is the aim of the project *Die zweisprachige Edition der Dioptra (P 35902)* funded by the Austrian Science Fund FWF. The preparation of an automatically annotated and manually post corrected version of this text will benefit further research as it provides authentic Middle Bulgarian training data for similar projects.

In my talk, I want to show how not only further projects can benefit from this resource, but also how such an annotated text can shed new light on certain phenomena in the history of the Bulgarian language. More specifically, I want to show what one can learn about the historical evolution of long and short adjective forms and their distribution in the *Dioptra* by making it possible to apply corpus linguistics methods to a Middle Bulgarian text.

References

- Eckhoff, Hanne et al. (2018): „The PROIEL treebank family: a standard for early attestations of Indo-European languages.“ In: *Language Resources and Evaluation 52 (1)*, pp. 29–65.
- Eckhoff, Hanne/Berdičevskis, Aleksandrs (2015): „Linguistics vs. digital editions: The Tromsø Old Russian and OCS Treebank.“ In: *Scripta & e-Scripta 14-15*, pp. 9–25.
- Maion, Fabio (2022): „Wege zur verbesserten automatischen Annotation des mittelbulgarischen Kirchenslawischen.“ In: *Scripta & e-Scripta 22*, pp. 365–390.

KINETICS OF SARS-COV-2 ENTRY INTO CELLS

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SARS2-CoV-2 virus causing the COVID-19 disease led to a pandemic of worldwide proportions the effects of which are still present and felt today both socially and economically. As of present, more than 689 million people have been infected of which the official death cases are 6,89 million. A lot of research has been done on the virus and many insights of its structure and reproduction cycle have been revealed yet the detailed mechanism and dynamics of entry into cells still remains unclear.

Herein, we have studied the mechanism which the virus uses to infect the cells. We have taken advantage of the state-of-art live-cell microscopy and labelled viral like particles, to measure the dynamics and to unravel the mechanism of SARS2-CoV-2 entry into host cells.

COVID19 AND LYMPHOMA WITH SKIN LOCALIZATION

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The 2019 novel coronavirus (2019-nCoV), currently known as SARS-CoV-2, is the cause of coronavirus disease 2019 (COVID-19). Many of the clinical manifestations of SARS-CoV-2 infection are related to virus-induced disruption of the immune system and resulting tissue damage. As a result of immune system dysregulation after COVID-19, the unrestrained release of proinflammatory cytokines, elevated cytokine levels, and circulating chemokines cause hemorrhage, thrombocytopenia, and systemic inflammation.

Cutaneous T cell lymphoma (CTCL) is a spectrum of lymphoproliferative disorders caused by the infiltration of malignant T cells into the skin. Despite recent advances, CTCL remains challenging to diagnose.

We present a clinical case of a 63-year-old patient who was treated in the COVID unit of the Clinic of Internal Diseases of UMHATEM "N.I. Pirogov" on the occasion of a proven coronavirus infection with a PCR positive test for SARS-CoV2-virus, clinical symptoms of severe coronavirus pneumonia, and with accompanying disease - lymphoma with skin localization, condition after lower right lobectomy, chemotherapy and checkpoint therapy for squamous cell carcinoma of the lung. We also examined the role of the transcription factor NF-kB in the course and course of the coronavirus infection in a patient with the indicated lymphoproliferative disease and a history of active smoking.

The described clinical case is an interesting example of the "nuances" in the clinical course of the coronavirus infection in neoplastic comorbidity and the possibility to predict the clinical course of Covid19 in CTCL. This, in turn, facilitates the replication of such patients given the immunological terrain, the expected more severe course of the disease - early hospitalization, optimal prevention of the development of a "cytokine storm" and intensive monitoring and follow-up of such groups of patients is an imperative strategy for a better outcome of the disease.

COVID-19 AND CLL (chronic lymphocytic leukemia)

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Coronavirus disease 2019 (COVID-19) is a highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Factors aggravating the course of the disease are accompanying disorders such as cardiovascular diseases, diabetes mellitus, diseases of the respiratory system, oncological diseases.

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in the western world and is due to the accumulation of mature B lymphocytes in the peripheral blood, bone marrow and secondary lymphoid organs.

We present the course of the coronavirus infection in patients with an accompanying malignant disease, chronic lymphocytic leukemia (CLL), namely. The study included 8 patients with proven PCR positive tests for SARS-CoV2 and confirmed chronic lymphocytic leukemia as comorbidity, who were treated in the COVID unit of the Clinic of Internal Diseases of UMHATEM "N.I. Pirogov" The course of the coronavirus infection in the CLL group was compared with that in the control group of 100 patients. In both groups, we compared subjective complaints such as tiredness, fatigue, joint and muscle pain and objective criteria such as temperature, laboratory markers of inflammation, X-ray imaging and frequency of necessary intubation.

Despite the expected poor prognosis in patients with concomitant oncological disease, in the case of chronic lymphocytic leukemia our results showed a quite different milder coronavirus infection course. Obviously, patients with CLL cannot develop pronounced cytokine storm, most probably due to certain immunosuppression related to the pathogenesis and drug treatment options for the comorbidity CLL.

The more severe course of the coronavirus infection in the patients in our control group seems striking and unexpected in terms of higher and more prolonged fever, higher laboratory values of inflammatory markers, more extensive lung parenchymal involvement and consequent longer hospitalization and more frequent intubation need.

STUDYING DNA-PROTEIN CROSSLINK (DPC) REPAIR PROTEIN KINETICS VIA LIVE-CELL MICROSCOPY AND MACHINE LEARNING APPROACHES

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DNA in eukaryotic cells is coated with proteins, forming highly compact and dynamic structure, termed chromatin. Interactions between DNA and proteins are important for numerous cellular processes, such as cell division, transcription, and replication. These interactions are mostly transient and dynamic, which ensures their timely completion and spatial coordination. However, proteins can be accidentally covalently linked to DNA molecules, giving rise to DNA-protein crosslinks (DPCs), which represent barriers to transcription and replication. As such, DPCs represent a type of DNA damage¹. A number of chemotherapeutics are based on the induction of DPCs in order to overwhelm cancer cells and trigger their death. Our team investigates the kinetics of key proteins involved in the repair of DPCs induced by chemotherapeutic agents. In order to comprehensively follow the repair process through time, we employ time-lapse live-cell microscopy. To precisely track protein dynamics, we employ a machine learning-based algorithm, which enables precise quantification of repair protein kinetics^{2 3}.

References:

1. Zhang, H., Xiong, Y. & Chen, J. DNA – protein cross - link repair : what do we know now ? *Cell Biosci.* 1–10 (2020). doi:10.1186/s13578-019-0366-z
2. Weigert, M. *et al.* Content-aware image restoration: pushing the limits of fluorescence microscopy. *Nat. Methods* **15**, 1090–1097 (2018).
3. Klein, S., Staring, M., Murphy, K., Viergever, M. A. & Pluim, J. P. W. elastix: a toolbox for intensity-based medical image registration. *IEEE Trans. Med. Imaging* **29**, 196–205 (2010).

DARK HOLES AT THE MICROSCOPIC LEVEL

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FUS (Fused in Sarcoma) and EWSR1 (Ewing's Sarcoma Breakpoint Region 1) are abundant RNA-binding proteins with multiple roles within the cell. They belong to the FET family proteins and possess the ability to undergo transient liquid-liquid phase separation (LLPS), a phenomenon that has an emerging vital role in both human health and disease. FUS and EWSR1 are known to accumulate rapidly in complex DNA lesions induced by laser ablation in living HeLa Kyoto cells [1]. Complex DNA lesions form micron-sized, phase-contrasted membraneless foci that require FET proteins. Interestingly, after the initial recruitment, FUS and EWSR1 are gradually excluded from the damage sites, replacing the proteins-enriched foci by a dark region.

In the present study, we demonstrate that the eviction of FET family members FUS and EWSR1 is a process independent of their accumulation and is a result of restriction of the access of the freely diffusive FUS and EWSR1 at the site of DNA damage. We show that interfering with post-translational modifications that play key roles in DNA repair, namely phosphorylation by ATM, ATR or DNA-PK, ubiquitination, acetylation by HDAC1/2, and methylation by EZH2, had no effect on FET protein exclusion. However, inhibition of transcription-related cyclin-dependent kinases (CDKs) efficiently diminished FUS and EWSR1 exclusion. Importantly, we also demonstrate that the active exclusion of FUS is required for the efficient accumulation of 53BP1 at DNA damage sites *in vivo*.

References:

[1] R. Aleksandrov, A. Dotchev, I. Poser, D. Krastev, G. Georgiev, G. Panova, Y. Babukov, G. Danovski, T. Dyankova, L. Hubatsch, A. Ivanova, A. Ategin, M. N. Nedelcheva-Veleva, S. Hasse, M. Sarov, F. Buchholz, A.A. Hyman, S.W. Grill, S. S. Stoynov, Protein dynamics in complex DNA lesions, *Mol. Cell* 69 (2018) 1046–1061, <https://doi.org/10.1016/j.molcel.2018.02.016>.

NEW STRUCTURAL MOTIFS OF SQUARIC ACID DERIVATIVES OF MINO ACIDS, AMINO ACID AMIDES AND DIAMIDES

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Design of new materials with second order nonlinear optical (NLO) properties in the bulk requires a strategy for obtaining non-centrosymmetric crystals and the employment of chiral agents (*e.g.* chiral counter ions) is a powerful technique for obtaining such crystals. Considerable progress has been made in recent years by controlling the assembly of individual molecules in solids, using hydrogen bonding as a powerful non-covalent force for organizing organic molecules. Squaric acid (H_2Sq) provides an attractive template for generating tightly hydrogen bonded self-assemblies from polarizable cations in general and basic amino acids in particular. During the last 20 years in our group series of non-centrosymmetric crystals have been synthesized, isolated spectroscopically and structural elucidated by means of the single crystal X-ray diffractions study. The possibility of this strong acid to stabilize both hydrogensquarate anion (HSq^-) and squarate dianion (Sq^{2-}) allows controlling its self assembly in the crystals and tuning their spectroscopic, optical and non-linear-optical properties. On the other side formation of squaric acid amides and diamides is another possibility to generate new organic materials with non-linear-optical application. The known up to now structural motifs are: (HSq^-) individual α -dimers (**Ia**) and two independent isolated α -dimers (**Ib**), HSq^- α -chains (**IIa**, **IIb**), HSq^- β -chains (**IIIa**, **IIIb**), differing by the disposition of the anion with respect to the chain. In **IIIa** all of the HSq^- are co-planar, while in **IIIb**, they are orientated in a mutually perpendicular manner. In the tetramer structural motifs (**IVa**, **IVb**, **IVc**), we can distinguish three known fragments, **IVa** with equivalent HSq^- anions disposed in a planar manner, **IVb** with equivalent HSq^- anions that are orientated in mutually perpendicular pairs, and the tetramer motif $\text{H}_2\text{Sq} \cdot 2\text{HSq}^- \cdot \text{Sq}^{2-}$ (**IVc**) consisting of different forms of squaric acid. Other motifs include $\text{H}_2\text{Sq} \cdot \text{HSq}^-$ double β -chains (**V**) and chains of α -dimers (**VI**), isolated (Sq^{2-}) dianions (**VII**), isolated hydrogensquarate anions (**VIII**) as well as fragments with $\text{HSq}^- \cdot \text{Sq}^{2-}$ moieties exhibiting a pseudo β -type of interaction (**IXa**) and with averaged disposition of the hydrogen atom between both the anion moieties and included solvent molecules (**IXb**). It is reasonable to expect that a further systematic variation of the counter ion in salts of the HSq^- and/or Sq^{2-} anions should lead to the isolation of additional novel self-assembly motifs and that these could exhibit interesting optical and/or non-linear optical properties.

INVESTIGATING THE INFLUENCE OF THE EXTERNAL ELECTRIC FIELD ON THE TAUTOMERISM IN 7-HYDROXYQUINOLINE DERIVATIVES

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Tautomerism, the reversible isomerization phenomenon in organic compounds, is pivotal in numerous chemical and biochemical processes. This study examines the influence of an external electric field on the tautomerism of 8-(benzo[d]thiazol-2-yl)quinolin-7-ol (HQBT), a derivative of 7-hydroxyquinoline (7OHQ), which serves as a notable example of long-range proton transfer (PT). In 7OHQ, PT is typically intermolecular and assisted by solvent or concentration, or it could occur after applying external electric field. Through structural modifications, HQBT, a *ножел* "proton crane" makes possible the true intramolecular long distance proton transfer. Density functional theory reveals that HQBT exists predominantly as an enol tautomer (off state) in the ground state. However, under the application of an external electric field, a significant intramolecular proton transfer occurs, shifting the proton to the quinolyl nitrogen atom (on state). This transformation is driven by the much higher dipole moment of the keto tautomer, suggesting that an external electric field can simulate the effect of a solvent in influencing tautomeric equilibrium. In the excited state, the stabilization of the polar on state inhibits further proton transfer, confining the system's dynamics to the conical intersection region. This research not only enhances the understanding of tautomer behavior under external fields but also provides innovative strategies for controlling chemical equilibria, with potential implications for various solution-phase processes *in vivo*.

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QUANTITATIVE ASSESSMENT OF THE INTERMOLECULAR INTERACTIONS BETWEEN FOLATE-BASED VECTORS AND THE FOLATE RECEPTOR- α

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Combating cancer requires development of efficient therapeutic methods such as targeted drug delivery. A class of active targeting drug delivery systems (DDS) relies on binding the drug to a vector that favours its delivery and release to specific types of cells by recognizing their cellular components. This approach is employed to trace computationally the behaviour of a promising ligand-receptor pair: folic acid and folate receptor- α (FR α), the latter being overexpressed on cancer cells surface [1].

The current study is focused on obtaining a quantitative assessment and establishing the dominant intermolecular interactions of ligand-receptor binding of folate and five of its structural analogues to folate receptor- α [2]. Statistical analysis and quantum mechanical calculations using Density functional theory (B3LYP/6-31G**) are carried out first, providing insight into the overall magnitude of the supramolecular interactions within the ligand-receptor complexes. This is then supplemented by computations with the Molecular Mechanics Poisson–Boltzmann surface area method to estimate the various contributions to the total interaction free energy.

The obtained results reveal that electrostatic attraction is the dominant share of the ligand-receptor interaction energy. The specifics of the binding of the separate ligands to FR α stem mostly from differences in the polar energy contribution. The dielectric constant of the surrounding medium has minor influence on the local ligand-FR α coupling. The obtained energy-based characterisation enables understanding of the relative stabilisation of the complexes of the separate vector ligands with the protein. This, combined with molecular dynamics modelling [1], allows outlining the most promising vector ligands for inclusion into active targeting DDS.

References:

[1] Petrova, J.; Gocheva, G.; Ivanova, N.; Iliev, S.; Atanasova, B.; Madjarova, G.; Ivanova, A. J. Mol. Graph. Model. **2019**, 87, 172-184.

[2] Schaber, E. N.; Ivanova, N.; Iliev, S.; Petrova, J.; Gocheva, G.; Madjarova, G.; Ivanova, A. J. Phys. Chem. B **2021**, 125(28), 7598-7612

ENCAPSULATION OF EUGENOL BY SPRAY DRYING USING SOLUPLUS® AND LUTROL F 127 AS SOLID CARRIERS

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Eugenol is a natural yellow liquid substance with a spicy aroma, found in clove oil, cinnamon, nutmeg, and basil [i]. It possesses antioxidant, antifungal, antibacterial, antiviral, and local anesthetic properties [ii]. Eugenol has various applications in the pharmaceutical and food industries, cosmetics, and in agriculture as a pesticide. It is also used in a mixture with ZnO as an endodontic sealer in dental medicine [iii]. However, since eugenol is practically insoluble in water [iv], its bioavailability is limited. Therefore, we significantly enhanced its water-solubility by encapsulation in the polymers Soluplus® and Lutrol F 127 using spray-drying technique. The formulations were optimized by the addition of the sweetening agent *myo*-inositol (a sugar alcohol, formed in the human organism from glucose) and the anticaking agent Aerosil® 200 (fumed silica). *Myo*-inositol could not only play a role of an excipient, but also finds application as a food supplement with medical benefits in patients with diabetes, insulin resistance, polycystic ovary syndrome, and metabolic syndrome [v]. Formulations with different percentages of eugenol (5, 10, and 15 %) with respect to the Soluplus® weight were obtained. The encapsulation efficiency was found to be highest ($98.2\% \pm 1.9$) in the case of the compositions with 5% eugenol. If Lutrol F 127 is included in the formulation, the encapsulation efficiency is notably lowered to ~ 84%, but a more pronounced spherical shape of the particles and improvement of the powder flowability are observed.

The compositions containing *myo*-inositol and Aerosil® 200 are considered as optimal in terms of encapsulation efficiency, overall amount of loaded eugenol, yield, and powder rheology.

References:

- Cortés Rojas, D.F.; de Souza, C.R.; Oliveira, W.P. *Asian Pac. J. Trop. Biomed.*, **2014**, 4 (2), 90.
Ulanowska M.; Olas, B. *Int. J. Mol. Sci.* **2021**, 22, 3671.
Abrishami, A.; Manjarrés, V.; Gutmann, J. L., *J Hist Dent* **2022**, 70(2), 107.
Budnavi S., ed., *The Merck Index*, 11th edn., Merck & Co Inc., Rahway, **1989**.
DiNicolantonio, J.J; O'Keefe J. H. *Open Heart* **2022**, 9, e001989.

3D FLOW FIELD DESIGN IN PROTON-EXCHANGE MEMBRANE HYDROGEN FUEL CELLS

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The performance and durability of proton-exchange membrane fuel cell are dependent by fuel delivery and water management. Unlike the traditional parallel and serpentine flow fields the 3D complex flow-field with repeating baffles along the channel induce a micro-scale interfacial flux between the GDL and the flow-fields which leads to water removal from GDL due to the dense oxygen flow. Another approach for channels form is Turing flow field design which inspired the natural occurring form such as leaves, lungs and blood vessels and enhancing the inlet flow significantly comparing with traditional design. Combine flow field design between the Turing flow field and repeating baffles along the channels are modeled and outcome performances are compared.

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