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THE CHANGING ROLE OF MATHEMATICS IN MEDICINE AND BIOLOGY IN THE 21ST CENTURY: AN ONCOLOGY PERSPECTIVE

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ABSTRACT

Mathematics has long provided the foundation for biomedical discovery — from dynamical systems and biostatistics to evidence-based medicine. In contemporary applications of mathematics, IT, and AI in medicine, the dominant challenge is increasingly one of **essential complexity** (in the sense of Frederick Brooks): the greatest difficulty lies not in the technology itself, but in accurately understanding and adequately modeling the intricacies of clinical reality. Modern tools such as machine learning (ML), retrieval-augmented generation (RAG), and MLOps practices reduce the *accidental complexity*, yet they cannot eliminate the intellectual effort required to design sound models. In other words, we have shifted from the era of asking "*how can we build it?*" to the era of asking "*what exactly should we build, and how should we model it correctly?*"

Breakthrough advances in AI and large language models (LLMs) are now delivering revolutionary tools that can raise diagnosis and therapy to unprecedented levels of quality. Examples such as the *Tsinghua AI Agent Hospital* demonstrate this transformative potential. Yet, the growing deployment of AI in medicine must confront the most critical challenge for contemporary AI: **trust in AI**.

In response, the University of Warmia and Mazury (UWM) and the National Oncology Institute (NIO–PIB) have launched a joint initiative, *OnkoBot* — an oncology-focused AI system with human-in-the-loop (HITL) supervision. OnkoBot is designed to support patients, enhance clinical decision-making, enable medical education and clinical auditing, and improve the overall safety of oncology care.

The OnkoBot project directly addresses two fundamental challenges for any non-trivial applications of mathematics, IT and AI to clinical medicine: *essential complexity* and *trust in AI*. OnkoBot is not just another chatbot; it ensures safe oncology use through uncertainty representation, justified reasoning, and HITL supervision.

This lecture outlines our framework for addressing these challenges in oncology, illustrated by the development of AI-based decision-support systems for prostate cancer diagnosis and treatment. Our objective is not to eliminate essential complexity or uncertainty in trust toward AI, but rather to *maintain them within acceptable bounds for clinical experts* through explicit representations of uncertainty, modular separation of concerns, verifiable reasoning, and human-in-the-loop collaboration. We propose mechanisms that simultaneously minimize uncertainty while maximizing explainability and ensuring alignment with regulatory requirements such as the MDR and AI Act, all under real-world clinical constraints.

The core of our approach lies in modeling medical knowledge via knowledge-representation systems based on granular computing (GrC) and, in particular, interactive granular computing (IGrC). These frameworks can also accommodate non-classical reasoning, including multi-valued, fuzzy, probabilistic, modal, and intuitionistic logics.

For especially complex applications, we recommend **IGrC**, which integrates informational and physical layers (e.g., clinical reality) through *composite granules (c-granules)* under explicit CONTROL — Risk Management (RM), Information Management (IM), Decision Management (DM), and Resource Management (ResM), i.e., the full spectrum of clinical decision contexts. This design grounds semantics in the physical domain and synchronizes language, reasoning, perception, and action. This continuous adaptation and synchronization of 'perception and action' takes place in a tight, iterative loop of collaboration with the medical expert, forming the core of the human-in-the-loop approach. From the perspective of rough sets, the focus shifts from approximating concepts to approximating *granules/solutions*, enabling approximate cognitive computations within real oncological workflows. Along these computations, approximate solutions to problems are constructed, e.g., concerning diagnosis or therapy. In this architecture, hallucinations are mitigated through evidence-linked granules, abstention policies, and provenance-based reasoning.

Based on the above considerations, we conclude that the core message of this lecture is a paradigm shift in the application of mathematics to 21st-century medicine. We are transitioning **from computational models that operate on numbers and aggregates (like vectors and matrices) to models of granular computing—particularly interactive ones—that work primarily with granular information (intuitively human-understandable knowledge units) and physical-world entities**. These models must undergo constant adaptation to meet the demands arising from the complexity of the modeled phenomena and concepts. This adaptability allows them to address the challenges of essential complexity and to build the trust demanded by modern medicine.