<u>Pauli Symposium</u> ***"Mathematics for Medicine (Against Cancer)"***

Wednesday, <u>22 July</u> 2026

<u>"Skylounge"</u> 12th floor Fak. Mathematik @ Univ.Wien, Oskar Morgensternplatz 1, 1090 Wien

Joint event of the WPI Workshop "MathMed_26) (20-22 July, Doron Levy et al)
and the WPI Workshop "BioMath_26) (22-24 July, Thierry Goudon et al)

9:45 – 9:50 *Welcome*: Norbert J. Mauser (director WPI @ U.Wien)

9:50 – 10:25 Doron Levy (U. Maryland)
CAR T Cell Therapy: what can we learn from math ?

10:30 – 11:00 Coffee Break

11:00 – 11:35 Angelika Manhart (U. Wien):
Modelling & predicting breast milk dynamics

11:40 – 12:15 Marie-Jose Chaaya (I2M, Aix-Marseille Univ.)
A Mathematical Model for PDAC Tumorigenesis, Stiffness and Axons Remodelling

12:20 – 14:00 Lunch

14:00 – 14:35 Morten Andersen (Roskilde Univ., Denmark)
Mathematical modeling of blood cancers, chronic inflammation and treatment

14:40 – 15:15 Alexander Anderson (Moffitt Cancer Center, Tampa, FL)
Mathematical Biomarkers of Adaptive Therapy Outcomes in Prostate Cancer

15:20 – 15:50 Coffee Break

15:50 – 16:25 Chiara Villa (CNRS @ U. Paris Cité)
Predicting the efficacy of CAR-based immunotherapy: an interdisciplinary approach

16:30 – 17:05 Heiko Enderling (U. Texas, MD Anderson Cancer Center)
Digital Twins in (Radiation) Oncology

<u>17h15 Reception (in the Skylounge)</u>

Abstracts:

Doron Levy

Title: CAR T Cell Therapy: what can we learn from math?

We model the distinct in vivo dynamics of donor-derived Memory Stem CAR T Cells and standard CAR T cells (Gattinoni et al., *Cell* 2026) with a novel approach of coupling a system of ODEs to a multi-type branching process. The entire cohort difference reduces to one parameter, the stem self-renewal probability, which sits on opposite sides of an analytically derived phase transition and accounts for both the low-dose efficacy and the observed clonal succession. A profile-likelihood analysis shows the data identify the supercritical-versus-subcritical regime rather than a precise value. Because the transition is a threshold, it suggests a categorical release criterion for manufacturing, and the same parameter accounts for the per-cell amplification that underlies the low-dose efficacy.

Angelika Manhart

Title: Modelling & predicting breast milk dynamics

Breastfeeding creates a feedback loop between milk removal by an infant or breastpump, and the stimulation of milk production. In this talk I will present and discuss a hybrid continuous/discrete mechanistic model that captures this process. The model is fitted to and tested against time-course data collected by wearable breast pumps. Model analysis allows to understand which pumping/feeding strategies lead to sustainable milk production, as well as how to optimize one's pumping/feeding strategy.

Marie-José Chaaya

Title: A Mathematical Model for PDAC Tumorigenesis, Stiffness and Axons Remodelling

Pancreatic cancer is one of the deadliest cancers, and despite decades of research, treatments remain largely ineffective. To make progress, scientists must look beyond the cancer cells themselves and examine everything surrounding them. This work uses mathematical models as a virtual laboratory to study two hidden forces that shape how pancreatic cancer grows: the nerves that infiltrate the tumor and the progressive hardening of the surrounding tissue. Nerves are not passive bystanders; some slow tumor growth, while others accelerate it. Meanwhile, tissue stiffening acts as armor around the tumor, making it harder for treatments to penetrate and be effective. By building mathematical models of these interactions, this work helps explain why the same treatment can succeed in one patient and fail in another and opens the door to more personalized therapeutic strategies.

Morten Andersen

Title: Mathematical modeling of blood cancers, chronic inflammation and treatment

Human blood cell production is maintained by hematopoietic stem cells (HSC) which give rise to all types of mature blood cells. Experimental observation of HSC in their physiologic bone-marrow microenvironment is challenging including malignant mutations of HSC. To investigate the significance of the interaction between the HSC, malignant HSC, the stem cell niche and chronic inflammation, we propose a mechanism-based mathematical model that takes into account several standard-of-care treatments as well as novel inflammation reducing treatments. The model was calibrated to individualized patient-data consisting of longitudinal hematologic and molecular measurements from several patient cohorts. We believe that this approach could have direct clinical relevance, offering expert guidance for clinical decision in terms of disease understanding and optimal treatment scheduling.

Alexander Anderson

Title: Mathematical Biomarkers of Adaptive Therapy Outcomes in Prostate Cancer

Adaptive therapy is an evolution-based treatment paradigm has been shown to delay resistance in prostate cancer through treatment breaks that control, rather than minimize, tumor burden. However, patient responses are highly heterogeneous, and there is a significant unmet clinical need for biomarkers to personalize treatment scheduling. We develop and retrospectively validate mathematical biomarkers that predict time to progression (TTP), mean daily dose (MDD), and overall survival (OS) under adaptive therapy from first-cycle prostate-specific antigen (PSA) dynamics.This retrospective modeling and validation study utilized longitudinal clinical trial data from 2 independent cohorts: 45 patients with castrate-sensitive prostate cancer (CSPC) and 13 patients with metastatic castrate-resistant prostate cancer (mCRPC). Patients received either intermittent androgen deprivation therapy (for CSPC) or adaptive abiraterone acetate (for mCRPC). The initial treatment cycle served as the exposure period to extract longitudinal PSA kinetics. Mechanism-based mathematical biomarkers (AT Score, expected TTP, and expected MDD) were derived from first-cycle PSA kinetics. Outcomes included in silico benchmarking experiments and retrospective validation against clinical TTP and OS. Performance was benchmarked against standard phenomenological PSA metrics (e.g., PSA nadir, time to nadir, and doubling time). In the CSPC cohort (N = 40), the AT Score derived from first-cycle data was highly prognostic for prolonged clinical TTP. In the mCRPC cohort (N = 13), the AT Score exhibited a strong rank correlation with clinical TTP and was associated with prolonged TTP. Analysis of long-term survival data in the mCRPC cohort demonstrated that both the AT Score and eTTP were significantly associated with prolonged OS, whereas standard empirical PSA metrics displayed no association with survival. Mechanism-based mathematical biomarkers derived from the initial-cycle PSA dynamics accurately predict patient-specific outcomes and survival, outperforming

traditional phenomenological PSA monitoring. We propose these accessible metrics as a mathematically informed decision-support framework to stratify patients into personalized treatment protocols.

Chiara Villa

Title: Predicting the efficacy of CAR-based immunotherapy: an interdisciplinary approach

Adoptive cell therapy, also known as cellular immunotherapy, aims at enhancing the cancer-fighting capabilities of the patient's own immune cells. A promising approach is to genetically engineer immune cells to express a synthetic receptor, namely a chimeric antigen receptor (CAR), capable of targeting specific antigens (e.g. the MET receptor) expressed by cancer cells. Despite the potential of CAR-based immunotherapy to achieve durable clinical responses, a key obstacle to its efficacy is posed by antigen expression heterogeneity both within the same tumour and across patients. In this talk I will show how mathematical modelling, integrated with experimental data, can help predict the efficacy of CAR-based immunotherapy against antigen expression-heterogeneous tumours.

Heiko Enderling

Title: Digital Twins in (Radiation) Oncology

To give the right treatment at the right time to the right patient is the mantra of personalized medicine. A framework that could facilitate personalized therapies is the so-called digital twin. I present the latest developments in mathematical and computational modelling in radiation oncology to develop digital twins. To personalize cancer radiation therapy, we must give the right dose and dose fractionation, at the right time, dynamically adapted, to best harness the radiobiological effects of radiation as well as synergy with the patient's immune system. I present different simple approaches to build predictive pipelines and how to integrate those into clinical decision making towards the concept of real-time adaptive personalized radiation treatments. I will discuss past, present, and future clinical trials of such model-guided treatments.