Georgia Koppe

In the research group (RG) Computational Psychiatry, we focus on developing and applying advanced (multimodal) computational methods to model brain, physiological, and behavioral recordings and improve our understanding of altered cognitive functioning in psychiatric disorders, as well as to predict and identify effective personalized interventions.

My research is inspired by two long-term visions. The first vision is the ability to quantify human decision making and its underlying cognitive functions in terms of a set of interpretable and reliable (computational) parameters and features – akin to a cognitive profile - which elucidate the precise aberrant mechanisms underlying pathological states. To realize these goals, the RG has contributed to developing and improving statistical models aimed at reconstructing the dynamical system underlying time series data such as brain and behavioral signals (Koppe, Toutounji, Kirsch, Lis, & Durstewitz, 2019; Kramer, Bommer, Tombolini, Koppe, & Durstewitz, 2022; Schmidt, Koppe, Monfared, Beutelspacher, & Durstewitz, 2021). These models allow us to extract interpretable features believed to mechanistically implement cognitive (dys)function (as reviewed in Durstewitz, Huys, & Koppe, 2021; Durstewitz, Koppe, & Meyer-Lindenberg, 2019), and which thus differentiate between healthy and pathological states (Thome, Steinbach, Grosskreutz, Durstewitz, & Koppe, 2022). We are currently in the process of quantifying how network dynamics relate to a diversity of psychiatric symptoms and cognitive (dys)functions.

Beyond that, the RG has developed, validated, and applied behavioral computational latent variable models to quantify cognitive processes in different domains including operant learning, intertemporal decision making, and social interactions, in terms of physiologically interpretable parameters (e.g., Koppe et al., 2017; Linke et al., 2020; Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022). Moreover, we have recently developed an (online) framework which leverages mechanistic latent variable models to manipulate and tune experiments, with the goal of inducing experimentally predetermined choice frequencies on the single subject level (Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022). By applying the framework to induce graded choice frequencies (that is, behavior on a dimensional level), it warrants the dimensional investigation of cognitive functions and, from a neuroscientific angle, enables to resolve the associated neural response on a fine-grained level. Importantly, the procedure allows to identify valid behavioral models underlying human choice by formally comparing predicted to observed choice frequencies. For this validation, we draw on formal concepts from statistical learning theory and machine learning. To name a concrete example, we have recently made use of this framework to identify the most valid delay discounting model underlying intertemporal choices. The inferred model was then leveraged to generate an experiment in which the experimental trials induce discounting (choice) frequencies of .1, .2, .3, .4, .5, .6, .7, .8, and .9. The selected model was highly valid, its recovered parameters remarkably reliable, and model selection was replicated in 5 independent experiments (Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022). The framework itself is easily extendable to different cognitive domains which we are currently working on.

Two proximal clinically oriented goals w.r.t. this framework are the development of a holistic decision making model in the context of choices underlying pathological substance use (planned in collaboration with Prof. Dr. Kirsch and Prof. Dr. Sommer within subproject B08 of the TRR 265 for the following funding period), and the development of a gamified treatment approach which employs model-based artificial agents that steer personalized social interactions to enhance positive social experiences (grant application submitted together with Prof. Dr. Korn, UKHD).

By combining behavioral computational parameters with network dynamics features (as well as features from other modalities) and decoding their contribution to psychiatric symptoms and cognitive

(dys)function, we hope to gain a mechanistic profile predictive of individual pathological states, serving as an indicator for treatment.

My second long-term vision encompasses the opportunities posed by modern technologies such as wearable sensors and mobile devices for tracking mental health in real time in the context of daily life. Given the huge amount of information collected by these devices, it is conceivable to build predictive models which are capable of forecasting risks of experiencing psychiatric symptoms and maladaptive behavior, and use these forecasts to propose personalized interventions, as well as to educate users on personal behavioral contingencies associated with mental well-being (Koppe, Guloksuz, Reininghaus, & Durstewitz, 2019). One key benefit of such an approach is the ability to intervene in the (critical) moment and daily life context in which maladaptive behavior or altered experiences actually occur.

We are currently tackling this vision by means of three parallel project streams: In the current funding period of the TRR 265 (subproject A06), we develop predictive time series models based on recurrent neural networks which can effectively deal with different time scales and multiple modalities relevant to mobile health (mHealth) data (Kramer et al., 2022; Schmidt et al., 2021). Second, in the EU funded project IMMERSE (see key output points 6.2), I am leading a work package which is both concerned with enhancing efficacy of these models by data integration, as well as the development of a visualization dashboard which feeds back behavioral contingencies and their statistical implications to users and clinicians. The associated consortium is investigating whether this feedback may improve therapeutic outcomes in individuals with psychiatric disorders across Europe. Finally, and perhaps most importantly, in the living laboratory AI4U (see key output points 6.3), we implement our developed models into real world applications. For this, we established a virtual platform which projects and preprocesses incoming mHealth data onto the protected servers of the CIMH on a daily basis, trains our predictive models on these data, generates future forecasts by simulation, and based thereon, probabilistically selects personalized interventions deemed most effective for a given participant. This selection is then fed back to the ongoing application and presented to the user. We are currently in the process of testing the developed application among youth with the goal of preventing mental illness. The developments are combined with thorough evaluations of user experience and improved in a series of successive experiments (Rauschenberg et al., 2021). The general infrastructure setup in this project serves as a starting point for future extensions and conception of a prototype for a future medical device.

I strongly believe what makes both the short-term project goals and the above mentioned long term visions feasible and this RG unique is the continuous integration of knowledge from various fields including statistics, physics, medicine, psychology, and biology. This is mirrored in the diversity of students which apply and form part of the RG (ranging from physicists to physicians and psychologists), as well as in the active collaboration with researchers from various groups underpinned by grant funding (e.g., TRR 265 and please see key output 6). Interdisciplinary collaborations of members of this RG are further strongly encouraged and supported through me being an active fellow of a number of distinct initiatives and institutions which themselves are composed of very diverse researchers (e.g., the Heidelberger Academy of Sciences, the STRUCTURES excellence cluster on emergent phenomena in the physical world, the AI Health Innovation Cluster, and the Heidelberg Center for Interventional Network Neuroscience).

Key output of the years 2020-now.

1. The **development of a virtual platform (Backend) for training machine learning algorithms on mHealth data within a real time application**, with the aim of predicting and selecting effective

personalized treatments (here, in terms of ecological momentary interventions) based on simulation analyses. This achievement has been realized within a joint effort between the Department of Theoretical Neuroscience, the Department of Public Mental Health (Prof. Reininghaus), the IT department of the CIMH, and the commercial company movisens GmbH (see grant under output point 6.3). This RG's contribution consisted in setting up the IT infrastructure necessary to, e.g., integrate data interfaces, data preprocessing pipelines, as well as algorithmic inference, simulation, and feedback pipelines (implemented by PhD student Janik Fechtelpeter under my supervision). It provides a virtual environment and software infrastructure we can now build on in future studies to optimize predictive algorithms, participant feedback, and individualized treatment and risk prediction within real time mHealth applications (see also https://ai4u-training.de/)

2. The development of an (online) **framework for model-based experimental manipulation of behavior by (computational) behavioral latent variable models** inspired by concepts from statistical learning theory (Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022). We have successfully applied this framework to generate adaptive experiments, induce graded behavioral (and associated cognitive) intensities, and formally validate computational models of behavior, demonstrating high replicability. Our contribution lies in conceptualizing and implementing the entire framework along with all statistical derivations (implemented by Dr. Janine Thome under my supervision).

3. The **development of (multimodal) statistical methods for effective dynamical systems reconstruction** (Kramer et al., 2022; Schmidt et al., 2021), and the **application of these methods to discriminate between pathological and healthy states** (Thome, Steinbach, et al., 2022). My contribution here ranged from both deriving, implementing, and testing algorithmic features of the models, supervising students in doing so, and in applying these models to human data (together with former RG members Daniel Kramer and Philine Bommer, as well as Dr. Janine Thome).

4. The ongoing **development of a dashboard for feedback of mental health variables to clinicians and service users** within a mHealth application prepared in agreement with medical device regulations in the context of psychiatric healthcare (see grant under output point 6.2). Our task here was to contribute both easily interpretable visualizations and robust statistics, as well as guide the implementation of these variables into a commercial company application (conducted by PhD student Manuel Brenner under my supervision).

5. Establishment of **good scientific practice principles** as demonstrated via study preregistration in which we were conceptually involved (e.g., Owusu, Reininghaus, Koppe,

Dankwa-Mullan, & Bärnighausen, 2021; Pinger et al., 2022; Thome, Pinger, Durstewitz, et al., 2022; Thome, Pinger, Halli, et al., 2022), the public provision of analysis code for *all* published studies (in which an RG member is first or last author), uploading analyzed data features or original data as far as data privacy permits, and publishing in open access journals and conferences.

6. The **successful acquisition of funding** to equip this young RG with a critical number of PhD students. Among these grants are:

6.1 Verschwörungstheorien, Alternativmedizin und Parawissenschaft – wirken Heterodoxien individual stabilisierend in einer instabilen Welt? (Heidelberger Academy of Sciences; funding period: 01/2021-12/2023)

6.2 The implementation of Digital Mobile Mental Health in clinical care pathways: Towards person-centered care in psychiatry (EU Horizon 2020; funding period: 04/2021-03/2025)

6.3 Reallabor Künstliche Intelligenz für digitale personalisierte psychische Gesundheitsförderung bei jungen Menschen (MWK; funding period: 01/2021-12/2023)

7. **Publication of review articles specifically addressed to a wide scientific audience** to convey the general ideas and concepts underlying methods developed in this RG, including an elaborate review on the relevance of network dynamics to psychiatric dysfunction (Durstewitz et al., 2021), as well as on machine learning algorithms such as deep neural networks for (precision) psychiatry (Koppe, Meyer-Lindenberg, & Durstewitz, 2020).

8. My most important output within the last two years is **my daughter**, born early in 2021. My main contributions here lay in giving birth and keeping her alive, in close collaboration with her father. My daughter has had remarkable effects on the mental health of her grandmothers and grandfather, as well as other relatives, and may therefore be considered a highly successful and individualized therapeutic intervention.

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