Patient-specific point-of-care system for rapid combination therapy of fungal infections- *Mykopoint*

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Infections with resistant microorganisms are one of the biggest challenges for global health (O'Neill, 2014). While bacterial infections and resistance are high on the political agenda, the diagnosis and treatment of fungal infections is often neglected. Yet the total number of annual deaths is comparable to that of malaria, tuberculosis or HIV - possibly even higher. It is estimated that around 6.5 million people worldwide are infected by acute, life-threatening fungal pathogens every year, resulting in around 3.8 million deaths. At least 2.5 million of these deaths are directly attributable to the fungal infection. One of the reasons for the high mortality rates is the current slow initiation of therapies, which currently requires 5-7 days after taking a patient sample to select the antifungal drug. The health risks associated with fungal infections are increased by the rise in resistance to antimycotics, which can be directly linked to the extensive use in prophylaxis, therapy and agriculture. (Denning, 2024)

The *Mykopoint* process has been developed to address this unmet medical need and is based on the concept of fully automated, simultaneous testing of the efficacy of at least two antifungals in a patient sample in a single process step. Using flow simulations, a method was developed to generate dynamically overlapping drug gradients within two hours. Compared to conventional methods, the propagation time of drug gradients is drastically reduced. Additionally, all possible drug combinations and concentration gradients can be analyzed simultaneously.

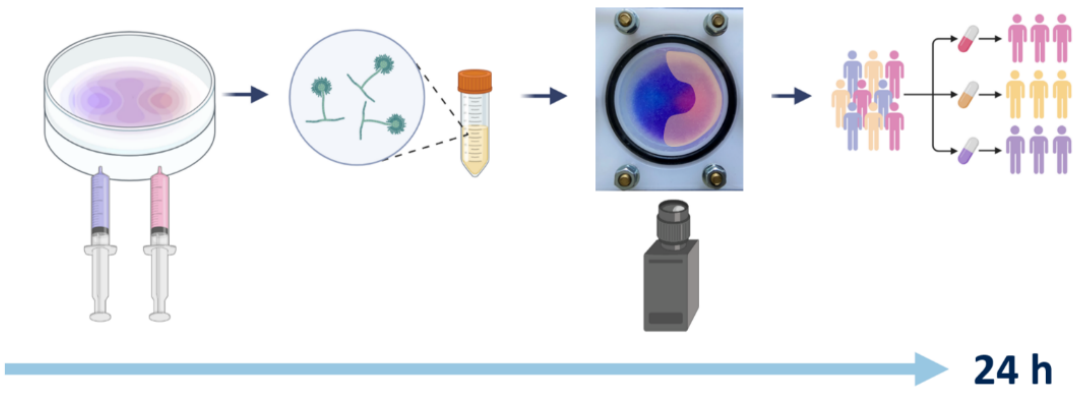

Figure 1: Schematic overview of the testing procedure: Formation of overlapping gradient fields in microfluidic bioreactor, application of fungal probe, automated visualization of fungal growth and resulting personalized treatment recommendations. Created with BioRender.com

The growth of the pathogens can be automatically analyzed and evaluated, allowing us to assess the effectiveness of the antimycotic therapy. A first prototype of the bioreactor has been built and the formation of gradient fields in an agar plate has been numerically simulated and experimentally visualized. The aim of the ongoing *Mykopoint* project is to deliver fully automated, personalized treatment recommendations within 24 hours, enabling customized, patient-specific therapy.

Denning, D. W. (2024). Global incidence and mortality of severe fungal disease. *The Lancet Infectious Diseases*, *0*(0). https://doi.org/10.1016/S1473-3099(23)00692-8

O'Neill, J. (2014). Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. *Wellcome Trust*.