

Dynamic Holographic Speckle Imaging for Antimicrobial Susceptibility Testing

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Abstract: Bacterial infections are responsible for 1 in 8 global deaths, which is the second-highest number of deaths worldwide, according to a study conducted by the University of Oxford.^[1] Based on the National Institute of Health, the traditional antimicrobial susceptibility testing, which can take up to 24 hours, often delays essential treatment.^[2] We have developed a label-free dynamic holographic speckle imaging system, which can perform antimicrobial susceptibility testing in 2 hours with minimal isolate preparation, enabling healthcare professionals to provide effective treatment to patients in a timely manner. In contrast to conventional speckle measurement, where the intensity is measured as $I = |S|^2$ (with S representing the scattering field), holographic speckle imaging utilizes a different approach. In hologram, the intensity is measured as $I = |R+S|^2 = |R|^2 + |S|^2 + R^*S + RS^*$, where R represents the reference beam field, and * stands for the complex conjugate. In holographic speckle imaging, what is important is the interference term R^*S or RS^* , which becomes significantly stronger than $|S|^2$ when a strong reference beam is used and the scattering intensity is weak. This interference term provides valuable information about the dynamic changes in the scattering field (S) induced by the motion of bacteria within the sample. Compared to the limit of detection of existing antimicrobial susceptibility testing methods, which is typically 10^5 CFU/ml, our system can determine antimicrobial susceptibility of bacteria at low concentrations of only 10^3 CFU/ml, which is 2 orders of magnitude lower compared to standard broth microdilution, enabling direct detection and early diagnosis with faster antimicrobial susceptibility testing and minimal isolate preparation. Our methods promise to facilitate bacterial infection treatment by providing an efficient and effective solution for healthcare professionals.

[1] Nuffield Department of Medicine, University of Oxford. Bacterial infections linked to one in eight global deaths, according to gram study.
[2] Gajic, I., Kabic, J., Kekic, D., Jovicevic, M., Milenkovic, M., Mitic Culafic, D., Trudic, A., Ranin, L., & Opavski, N. (2022). Antimicrobial Susceptibility Testing: A Comprehensive Review of Currently Used Methods. *Antibiotics* (Basel, Switzerland), 11(4), 427. <https://doi.org/10.3390/antibiotics11040427>