ABSTRACT

Time-lapse microscopy now enables detailed imaging data generation and monitoring of dynamic cellular processes at the single cell level. Recent studies have highlighted the usage and importance of this technology for investigating biological noise in gene regulation, cell growth and proliferation etc. Mathematical and statistical model development is of growing interest in capturing and testing hypothesis regarding the dynamical behavior of biological systems. Modeling bacterial communities forming biofilms relies on the efficient and accurate extraction of information from time-lapse microscopy data (image frame sequences) of growing bacterial colonies. However, the analysis of such "cell movies" data is currently very time consuming and error prone since it is essentially performed by human-experts. In this thesis we address this important limitation in a multi-resolution image analysis framework.

We have developed a methodology for identifying accurately the boundaries of individual bacterial cells and tracking them from frame to frame so as to construct the cells’ genealogy (bacterial cell segmentation and lineage tree construction) even in large-size microbial communities where there is great difficulty in identifying the individual cell boundaries. The automated and novel pipeline of algorithms we have developed combines methods from image processing and machine learning to segment and track bacteria precisely.

The pipeline has been tested and evaluated with two different cell movies datasets and several images produced by different labs. The developed methodology has been shown to achieve high F-measure score (above 95%) in each evaluation case. It can be applied to different image modalities, such as phase contrast, bright field, and fluorescent, produced by optical and confocal microscopy. Using extensive experimentation we demonstrate the robustness and reliability of the proposed pipeline regardless of the image modality used. Our image processing pipeline is fully automated, computationally efficient and suitable for high throughput analysis of bacterial cell movies without any human intervention on its calibration.

SUBJECT AREA: Image Analysis and Machine Learning

KEYWORDS: bacterial segmentation, cell counting, cell lineage construction, cell feature extraction and visualization, expectation-maximization.