Simulated movies of fluorescently stained bacteria

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Simulated biomovies of fluorescent cells were created by employing cell simulation based on shape, texture, growth and motion information. They are depicted in fluorescent channels where noise and other artifacts were additionally modeled. While the original cell simulation software [1] has been extended for biomovie simulation, the step for bacterial growth simulation is similar to image simulation. First, the cell shape is calculated. Second, the cell position on the image grid is calculated. Third, the cell texture is added. Fourth and last step, imaging artifacts and noise are added to the final image. For the simulated fluorescent biomovies, *bacterial* shapes are modeled as ellipses with varying length of semi-major and semi-minor axis. The bacterial cell positions are determined on a frame-by-frame basis by minimizing an energy function. For the first frame an initial bacterium is placed in the image center. After bacterial division, the new bacterium is placed next to the bacterium of which it originated from. After all bacteria for the frame have been calculated, both the position and shape of bacterial cells are input to the following energy equation:

$$E^*(bacteria) = \sum_{o}^{N_o} \sum_{p \in o} I_{dist}(p) + k * \sum_{o_1 \neq o_2}^{N_o} \sum_{p_1 \in o1} \sum_{p_2 \in o2} \delta(p_1, p_2) \qquad (1)$$

Where:

N_o	number of bacteria
I_{dist}	distance transformed mask of the bacterial cell shape
$\delta(p_1, p_2)$	equal to 1 if the below condition is fulfilled.

If $p_1 == p_2$ pixels of bacterium o_1 and o_2, respectively. Else, $\delta(p_1, p_2) = 0$.

The first energy summand helps bacteria remain together towards the image center. The second energy summand prevents overlaps between adjacent bacteria. The factor k weighs the energy term one against the second energy term. The gradient descent method is applied in order to to iteratively minimize the

energy equation to find the most optimal positions of bacterial cells on the current frame. Their positions in the previous image frame are the starting point for energy minimization in the current frame. Three fluorescent channels are simulated with varying appearance modeling the properties of various real fluorophores. The bacteria texture is calculated with the sigmoid function, defined as

$$f_{sigmoid} = \frac{I_i}{1 + e^{\kappa * v}} \tag{2}$$

I_i	maximum intensity of the texture of bacterium i (Gaussian distributed)
v	distance transformation value for the corresponding pixel on the mask
κ	controls the slope of the intensity at the bacteria edges

The movies referenced herein can be downloaded from `https://10.4119/unibi/2915541`. Simulated movies DS1, DS2, DS3, and DS4 contain a single green channel showing a medium intensity level and variability. The simulated movie DS5 has three channels with different properties stored in each RGB channel. The bacterial intensity is highest in the blue channel with the lowest variability. The green channel has the same properties as in the movies DS1, DS2, DS3 and DS4 which are medium intensity level and medium variability, respectively. The red channel has the lowest intensity and the highest variability. Each channel depicts linearly increasing background intensity values from the left to the right side of a modeled cell to simulate illumination inhomogeneity. This slope of the intensity ramp is chosen to be increasing from blue channel over the green channel to the blue channel. Gaussian noise is added with increasing level from blue channel over the green channel to the red channel.

References

[1] Wiesmann V, Sauer T, Held C, Palmisano R. and Wittenberg T. *Cell Simulation for Validation of Cell Micrograph Evaluation Algorithms.* Biomed Tech (Berl). September 2013. PMID: 24042916