# 科学研究費助成事業 研究成果報告書



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研究課題名(和文) Deciphering the bacterial cell division machinery using advanced imaging methods

研究課題名(英文)Deciphering the bacterial cell division machinery using advanced imaging methods

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研究成果の概要(和文):高分解能蛍光顕微鏡を用いて細菌細胞分裂の調査を行った。顕微鏡法とナノ加工法の組み合わせでは、細胞を直立位置に配置してイメージ化した。この見解変更からより優れた解像度が可能となり、その結果、それぞれのイメージからさらに多くの情報を得ることができた。次に細胞分裂機構がどれだけ頑強であるかを調べるために、ハート形、星形、正方形など不自然な形に変形させ観察したが、細胞分裂機構は特に膜形状の変化に敏感ではないという結論に至った。

## 研究成果の学術的意義や社会的意義

Advancement of our general understanding of bacterial cell division has lead to better possibilities to develop new antibiotics.

研究成果の概要(英文): Bacterial cell division was examined using high resolution fluorescence microscopy. In a combination of microscopy and nanofabrication approach were cells placed in a standing position and imaged. This change of perspective made it possible to achieve better resolution and, in that way, extract more information from each image. In a second step was cells reshaped into unnatural shapes like heart, stars and square to investigate how robust the cell division machinery is. We conclude that the cell division machinery is no sensitive to changes in the membrane geometry.

研究分野: Cell division, fluorescence Microscopy

キーワード: Drug development Microscopy Bacteriology

#### 1. 研究開始当初の背景

Bacteria are single celled organism that can cause disease. With the increase of antimicrobial resistance do we need to develop new therapeutics.

#### 2. 研究の目的

The aim of this research was to obtain a better overall picture of the bacterial cell division machinery. We also wanted to better understand how robust the division machinery is. We questioned if we could disrupt the assembly of the machinery at midcell by distorting the cell shapes, and transformed them into various non-natural shapes.

This because the bacterial cell division machinery is a highly attractive target for new antibiotics.

### 3. 研究の方法

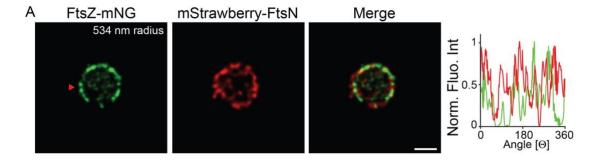
Super-resolution fluorescence microscopy and cryo-electron microscopy in the gramnegative bacteria E. coli.

To change the perspective of imaging cells were a nanofabrication approach applied, where micron sized pillars were fabricated. These pillars were used as a mold to make holed in soft agarose pads, in which cells were trapped in a standing position.

#### 4. 研究成果

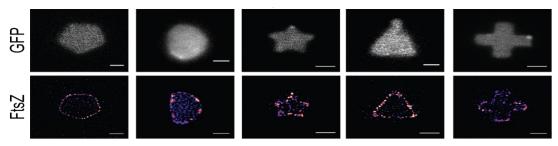
In this project I was able to:

• Show that certain divisome proteins form rings with different radii during membrane constriction and cell division.



The figure show two different cell division proteins tagged with fluorescent proteins and trapped in a standing position. FtsZ is in green and FtsN is in red. The intensity plot to the right indicated that the two proteins did not colocalize in the circumferential direction at all times.

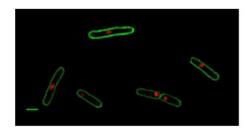
• Show that FtsZ, the major cell division protein, is not sensitive to the underlying membrane curvature when assembling at midcell.

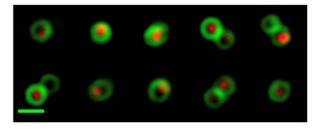


The figure shows *E. coli* cells that were reshaped into various shapes. Cells were transformed to express GFP in the cytoplasm, upper row. Then, cells expressing FtsZ-mNeonGreen were reshaped in nanocages. As clearly can be seen can cells be reshaped

into various shapes and FtsZ can assemble at midcell in those cells.

• Show that MatP can bind to *E. coli* inner membrane lipids after cell division is finalized.





The figure show MatP(red) localization in cells laying down and standing up in micron sized holes. Green is representing the membrane (mNG-GlpT). MatP predominately localized in close proximity to the membranes.

Overall, together does these findings advance our general understanding of the bacterial cell division machinery. This knowledge may be used when developing new approaches to search for novel therapeutics and antimicrobials.

- 5. 主な発表論文等 〔雑誌論文 4件〕.
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  The bacterial DNA binding protein MatP involved in linking the nucleoid terminal domain to the divisome at midcell interacts with lipid membranes. *mBio*. 2019.

  April. Accepted. IF. 6.689. (peer-reviewed)
- (2) **Söderström B.** \*, Chan H. and Daniel O. Daley\*.

Super-resolution images of peptidoglycan remodelling enzymes at the division site of *Escherichia coli. Current Genetics*. 2019 Jan. 65(1): 99-101. IF. 3.574. (peer-reviewed)

(3) <u>Söderström B.</u><sup>#</sup>, Badrutdinov A., Chan H., and Ulf Skoglund.

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*'Featured Image'* on Nat. Comms. homepage Dec18/Jan19. This publication was featured in "Scientific American".

(4) <u>Söderström B.</u>\*, Chan H., Shilling P., Skoglund U. and Daniel O. Daley\*. Spatial separation of FtsZ and FtsN during cell division.

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- (1) EMBO workshop on Bacterial cell division, Lund, Sweden Bill Söderström. The Z-square. 2019.
- (2) IMC19, Sydney, Australia

  <u>Bill Söderström</u>. Super resolution approaches to study

  Bacterial cell division. 2018
- (3) ITQB, Oeiras, Portugal Bill Söderström. Cell division in *E. coil*. 2018
- (4) Stockholm University, Stockholm, Sweden <u>Bill Söderström</u>. Super resolution approaches to study Bacterial cell division in vertically trapped cells. 2018
- (5) Winter Q-Bio., Maui, Hawaii <u>Bill Söderström</u>. Internal organization of the *E. coli* cell division machinery and its spatial regulators. 2018
- (6) UTS, Sydney, Australia Bill Söderström. Cell division in *E. coli*: From Initiation to completion. 2017
- (7) IUMS, Singapore

  <u>Bill Söderström</u>. The bacterial cell division machinery is built in modules. 2017
- (8) Spanish National Center for Biotechnology, CNB, Spain <u>Bill Söderström</u>. Cell division through a new perspective. 2017
- (9) New Approaches in Microbiology, EMBO/EMBL Symposia, Germany Bill Söderström. Correlating protein localization with envelope constriction during cell division in *Escherichia coli* 2017