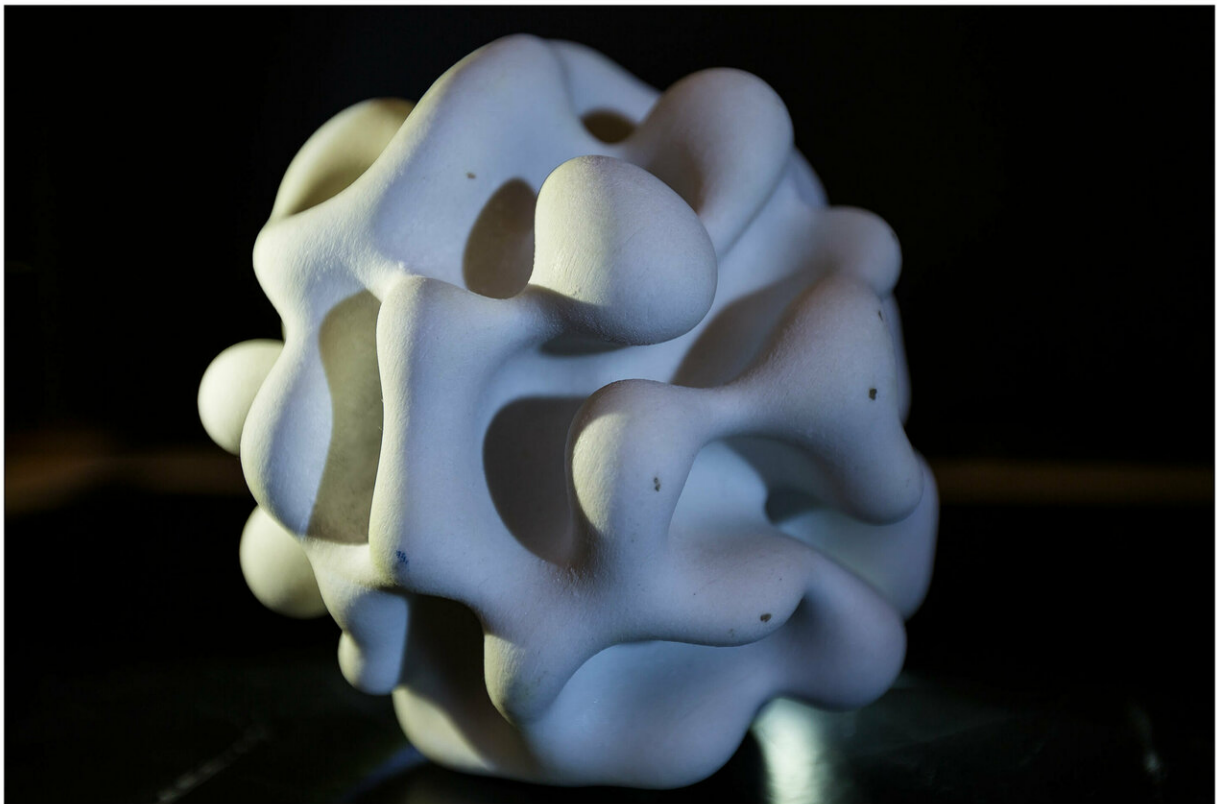# Mathematical model can improve our knowledge on cancer

January 16 2019

3D printed miniversion of a folded organ with many shallow folds. According to the mathematical model developed by the researchers, this happens when the cells divide fast, with rapid, off-balance growth of cells. Credit: Ola Joensen

Researchers at the Niels Bohr Institute, University of Copenhagen, have

developed a new mathematical tool to characterize what happens when cells lose their polarity (direction) in diseases such as cancer. The result is advancing the understanding of how the fertilized egg cell develops into a complete organism.

Biological shapes, like individual organs or an entire body, can be reproduced or maintained with great accuracy, just like in the embryonic development or during the adult stage. Multicellular organisms can develop highly complex structures that make up their tissue or organs and are capable of regenerating perfect reproductions of these structures after injury. This involves folding of sheets formed by groups of dividing and interacting cells. Although much is understood about some of the intermediate steps that occur during development and tissue repair, exactly how thousands of cells together work out what shapes they need to form remains unknown.

Building the mathematical model

"In this study, we wanted to see how cells organize into folded sheets and tubes, and how this process can be so precisely reproduced as is seen during development," says lead author Silas Boye Nissen, Ph.D. student at the Center for Stem Cell Decision Making, StemPhys, University of Copenhagen, Denmark. "To answer this question, we built a mathematical tool that can model two types of cell polarities and simulated how many cells organize themselves into folded sheets and organs."

The researchers found that by changing one of two polarities in the model, they were able to simulate a rich diversity of shapes. The differences in the shapes were dictated by two factors: The initial arrangement of the cells and external boundaries—such as the shape of an egg influencing the development of the embryo inside.

Colored print in plaster of a developed structure, formed by the cells initially being randomly embedded in a lump of cells. This structure is maintained by cell division or damage. The two printed figures are obviously very different, so the starting point for cell growth or the influence from outside, e.g. by boundaries, define the result, even though the growth is dictated by the same, relatively simple rules in the mathematical model. Credit: Ola Joensen

By exploring a multitude of theoretical scenarios in which the polarities were altered, the model was able to narrow down the focus to a few theories to be tested experimentally. In miniaturized versions of organs grown in the lab (called organoids), the model predicted that rapid, off-balance growth of cells will cause the growing organoid to develop lots of shallow folds, while external pressure caused by the medium on the

organoids will cause fewer, deeper and longer folds. This means the model can improve our understanding of how folded organs like the brain or the pancreas are formed.

Few, simple rules apply for the formation of biological shapes

"Our findings advance our understanding of how properties of individual cells lead to differences in shapes formed by thousands of cells," says senior author Professor Kim Sneppen, Director of the Center for Models of Life, CMOL, University of Copenhagen, and senior coauthor Ala Trusina concludes: "Our work suggests that body parts may not need detailed instructions to form, but instead can emerge as cells follow a few simple rules. We can now explore what happens if cells gain or lose their polarities at the wrong time or place, as often happens in cancer."

Provided by University of Copenhagen