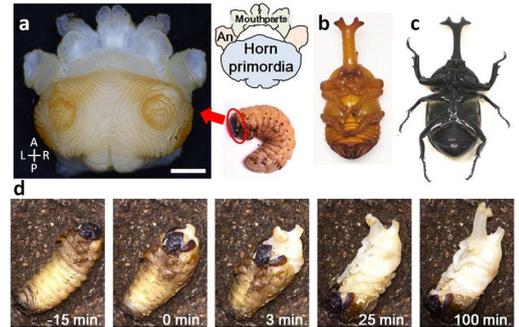


## 3D morphogenesis by 2D folding patterns

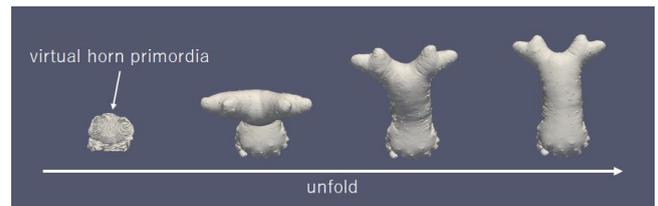
Organ shapes are directly linked to their functions. So “how is the shape of an organism determined” is an important question in biology. Previous studies have revealed many things about the functions of genes and cells that work in the process of morphogenesis. However, there is still a large gap between the macro spatial information, which is essential to the construction of the “three-dimensional shape”, and the microscopic behavior at cell levels.

To fill the gap, we focused on beetle horns as the new research materials. Beetle horn is formed as a compactly folded bag (horn primordia) in the larval head, and during molt, it expands like a balloon and turns into a large horn in a very short time. From this distinctive growth method, we thought that “horn morphogenesis” could be divided into the biological question of “where folds are made in cell sheets” and the physical question of “what three-dimensional structures are made by unfolding specific folding patterns”. Simplifying “horn morphogenesis” into 2 main questions has made it possible to fully understand how morphogenesis occurs.



In this paper, we first verified that biological factors such as cell proliferation and migrations are not involved in the process of expansion of horn primordia. We reconstructed the 3D data (virtual horn primordia) from serial frozen sections and expanded it using physical simulation. When unfolded, the virtual primordia became the shape of pupal horns. Since the virtual primordia had no cells, the transformation of horn primordia into pupal horns does not require biological factors, that is, the unfolding process is a simple physical process. In other words, the complex shape of a pupal horn is coded by folding patterns on

primordia. Next, the folding pattern of each place of primordia was unfolded by the simulation to clarify the relationship between folding patterns and 3D shapes. Through these computer experiments, we showed how the complex shape of pupal horns is made by these folding patterns.



In order to fill the large gap of our understanding between the functions of genes and morphogenesis, it is necessary to study morphogenesis from the viewpoint of both the biological factor and the physical factor. In most cases, these two factors occur at the same time dependent on each other. In this paper, we showed that these two elements can be considered separately in the process of horn formation. In addition, the concept of "two-dimensional pattern formation" and "three-dimensional morphogenesis", which have been extensively studied in the past, can be linked to each other by the new concept of "2D folding pattern codes 3D shape". We hope that developing this knowledge will allow us to design folding patterns that could create any 3D forms.

