Review of: "Morphomechanics: An Updated View"

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This article is on “Morphomechanics,” which (I think) is a mechanical theory to explain self-assembly in living matter. However, it’s not really clear to me - from this article - what Morphomechanics really is. Is it related to Morphoelasticity (e.g., see “The Mathematics and Mechanics of Biological Growth” by Professor Alain Goriely)? Is Morphomechanics supposed to describe the behavior of all active matter? Broadly speaking:

Consider providing more detailed examples or references to clarify the relationship between Morphomechanics and Morphoelasticity.

Consider specific improvements or additions to the sections discussing topological defects and mechanical stress to enhance clarity.

Some specific comments:

Section: At the core of morphomechanics
“Living matter may behave, to some extent, as a liquid crystal” - you could give some conditions under which living matter behaves like a liquid crystal. Are there specific tissues you have in mind?

The topology of defects could be explained more thoroughly. Defects in crystals represent a break in the symmetry of the crystal lattice, e.g., a missing atom in a copper crystal. Are biological defects similar? What exactly are we seeing in Figure 1?

Figure 2: What *is* the correspondence between topological defects and the body plan? This could be explained more concretely.

Section: Harnessing Defects
Give a reference for “active turbulence.”

Figure 3: What are we seeing here? Is it a thin nematic film that was originally shaped like a sphere and has developed protrusions? A “before” and “after” representation could help the reader. More explanation about how the defects “oscillate” between the tetrahedral configurations would also be helpful: the protrusions in Figure 3 do not seem to be in a tetrahedral configuration - they seem to lie in a plane. Do the oscillations dampen so that one particular configuration is eventually chosen?

Section: Measuring Mechanical Stress

First sentence: “Morphomechanics is based on the assumption that cells are capable of measuring the magnitude and duration of different mechanical forces.” I understand that ion channels allow cells to sense forces. But the examples don’t seem to illustrate how cells can measure the *duration* of forces, as claimed in the first sentence.

Section: Discussion

“As stressed by Levin and Martyniuk (2018), a main feature of a code is arbitrariness: the response triggered by a signal is not a physical consequence, but something arbitrary.” This sentence is very abstract and I’m not not sure what it means. Can you explain “code” and “arbitrariness” more concretely? Are you talking about a genetic code? Why is the arbitrariness important? In the example given, high temperature leads to protein denaturation. What is the “code” in this case, and why is denaturation “arbitrary”? Is it because the protein can take any shape?

Consider putting the section on differential strain in its own section. How tissues self-organize in response to stresses (and therefore strain) is a vast topic.

What does “SO” stand for in Figure 4?