

The authors attempt at defining comparative design rules for self-assembly, self-folding and origami. This is a grand challenge and I commend them on this lofty goal, mainly because there are thousands of academic papers where the words have been used with very different meanings.

The authors list a lot of "quotes" from literature and discussions of nomenclature. I feel that the nomenclature may be less important than giving the readers a clear understanding of the boundaries and capabilities of each field. I would note also that self-assembly is a commonly misused word, and aptly commented by Whitesides (Science 2000) in the section header, *"Is Anything not Self-Assembly"*. Also, I disagree with some of the definitions (discussed later), and I suspect that others may have other disagreements and it may take decades to resolve these issues.

The new experiments are very nice and have the potential to elucidate and validate some key principles or introduce new ones. But the paper should probably be better organized; possibly with sub-headers such as Definitions; New experiments; Discussion of findings from new experiments; Comparison to prior understanding; New concepts; Overall summary and discussions.

With respect to the definitions, I have some disagreement. My understanding of the three terms are as follows.

Self-assembly: The assembly of complex structures from elementary (less complex) building blocks without (much/any) human/robot intervention.

I use the word (much) because even in nature (e.g. protein self-assembly, there are often chaperones) so self-assembly is often "assisted" even in nature.

I disagree with the sweeping classification that self-assembly is parallel. In fact, hierarchy and sequential aggregation are common features of self-assembly. Hierarchy and sequence have aspects of "serial" processes. For example, by just mixing atoms together we cannot just self-assemble cities in parallel. There are combinations of parallel assembly of modules and then sequential assembly of modules in a sort of serial and hierarchical manner: (atoms form molecules); (molecules form cells); (cells form organs); (organs form humans); (humans form cities) etc. In prior work with self-folding polyhedra, similar features have been observed and reported. E.g. Planar nets first assembled/folded into stable intermediates (e.g. half dodec) and only then did stable intermediates assemble into polyhedra (full dodec).

To add to the confusion, the common use of the term self-assembly in the literature has been dominated by chemists / nanotechnologists who have used it mainly for aggregation of unconnected building blocks. As argued in published literature, it

would be extremely challenging to assemble a polyhedron with high yield using free-floating unconnected polygons. But, by connecting polygons in a net, one can significantly reduce the degrees of freedom, so self-folding is a nice trick to limit possible outcomes (the degrees of freedom). Interestingly, molecules use this trick, e.g. sp² and sp³ bonds have specific angles and constrain atoms in particular configurations to limit possible outcomes.

The authors have managed to assemble polyhedra from individual pieces, but this approach requires imposing constraints using other mechanisms (like using reaction vessels of specific sizes and shapes), and the yield obtained needs to be better discussed. Self-folding is similarly a class of self-assembly with constraints (e.g. tethered polygons).

Self-folding: A branch of self-assembly that involves folding. As alluded to above, self-folding can be seen as a trick in self-assembly to limit configurations in 3D self-assembly by incorporating constraints (permitting only bending and binding at specific points) within building blocks. Self-folding need not be serial since many panels can fold at the same time to form stable intermediates, then the stable intermediates can assemble into final structures much like self-assembly.

Origami: 3D assembly that involves folding of thin films (typically paper as per the Japanese translation) independent of whether human intervention is used or not. Typical origami does not allow cuts (kirigami) so the rules are somewhat restrictive. Many researchers have used the term loosely and interchangeably to mean self-folding, but this can cause consternation in traditional practitioners of origami art. In contrast to the strict terminological use of the word "origami", self-folding can use films with / without cuts and must not have (much) human/robot intervention.

As such this paper can be better organized, since it can be challenging to differentiate the findings from the new experiments vs terminology discussions. It is also unclear what new terminology is being introduced and what is merely being restated, often as quotations. It is also important to be careful while using words like "chaotic folding". Terms such as "chaos" have a very specific meaning.

In terms of the sections of new experiments, and discussion, of note, many of the design rules discussed in the paper have already been published including compactness, networks, manipulation of pathways for selecting isomers, degrees of freedom and stable intermediates. In this regard, the authors should clearly state what are validation experiments of previously published design rules and what are new rules/concepts being introduced here.

Also, one of the pressing challenges in the community today is to move self-assembly from the realm of philosophy and academic laboratory tinkering to real world manufacturing and engineering. When might humans be able to create self-assembling electronics / computers / furniture in a cost-effective manner at scale in an industrial setting? In this regard, dealing with defects are critical. Are there any new insights in this regard?

Finally, a minor but important point is to please describe experiments in enough detail (dimensions, materials etc.) that they could be reproduced in another laboratory. Also, where possible it is necessary to discuss yield (i.e. number of trials and outcomes) for statistical significance.