Re: *Skeletides: A Modular, Simplified Physical Model of Protein Secondary Structure*

Promita Chakraborty
QuezyLab, Palo Alto, California 94306, USA.
promita@quezylab.com

Abstract

This is a rebuttal of a paper titled *Skeletides: A Modular, Simplified Physical Model of Protein Secondary Structure*, published in January 2020 (Ahead of Print) and April 2020 (in-print) in the journal *3D Printing and Additive Manufacturing*¹. A formal complaint made provided no results. Despite my complaint to the Editor-In-Chief of the journal, Skylar Tibbits, in January, this paper went ahead and got published in print in April 2020 without proper citation, mention or acknowledgement of my work. Here I enlist the similarities between my work and this paper. Parts of this rebuttal have been reproduced from my prior blogposts about the problem^{2,3} explaining the details of the circumstances. In order to keep this paper in print, a proper attribution of my work is necessary, and an ethical thing to do (a list of citations is provided).

Details

There is an overarching similarity of language and methodology in this paper that suggests a strong inspiration from my work, but there is absolutely no mention of that. Authors mention several times about their work being a simpler version. However they never explain “simpler” to what? Or “simplifications” from what? “Simplified” form of what? That information is missing throughout the paper, a gross oversight of the foundational prior work they have built upon (my body of work⁴⁻¹⁰). Some examples of sentences from the paper:

- “The **simplified** model consists of amino acid units, which can be linked together ...”
- “To focus on these model elements, we made inherent **simplifications** with regard to ...”
- “We realized that there is a need for a new, **simplified** molecular protein model ...”
- “... and to **simplify** construction.”
- “Here, we set out to develop a new, **simplified** protein model that ...”

A few points on similarities:

- The layout of this paper has been taken from my publications, including all section names and layouts.
- The naming of the model(Skeletide) sounds similar to (and rhymes with) my model name(Peppytide).
- This paper is essentially describing a simplified version of my model, with more coarse-graining, using straight lines instead of atoms. (including the scaling

approximation – mine is 9.3mm/Å. vs theirs at the similar scale, only slightly modified, of approx. 7mm/Å)

- The authors mention that their model is a *simpler* version, but there is a glaring absence of the source of this approach to protein modeling, in order to mirror Angstrom level biophysical forces in protein folding (my body of work).
- Authors use the technique developed by me for designing, 3D printing, making, assembling and analyzing the model. Moreover, as in my models, the focus is on folding and on secondary structures.
- 8,000 PDB files have been used for analysis in this paper, a subset of what I had used before (78,000 PDB files). The data extraction process and python scripting for the PDB file formats is based upon my work.
- Citation needed: In Section *Turn Piece*, “a hinge design was implemented, which allows the ...” – This sort of hinge design is already published in my paper on [PeppyChain](#)⁷ (Chakraborty P. **PeppyChains: Simplifying the assembly of 3D-printed generic protein models**. Arxiv 2015. arXiv:1605.04166).
- Authors have used something called pseudo-Ramachandran plot (c-alpha vs. dihedral) to highlight regions of alpha-helix and beta-sheet activity. This approach is similar to what I had used in my work: Ramachandran plot (the two dihedrals, phi vs. psi) to highlight regions of alpha-helix, beta-sheet, pi-helix and left-handed helix activity.
 - Authors: “Similar to how peptide conformation can be fully described by analysis of the monomer dihedral angles in a Ramachandran plot, a protein ...”
 - A more accurate narration would be:
 - “Chakraborty’s Peppyptides were based on how peptide conformation can be fully described by analysis of the monomer dihedral angles in a Ramachandran plot, calculated from about 78,000 PDB files, from which the rotational barriers of the dihedral angles were calculated for alpha helix and beta sheet conformations and implemented with magnet arrays. Similar to that analysis, a protein ...”
- Authors focus on alpha helix (red), beta sheet, both parallel and antiparallel (blue), turn (black) structures. This is a subset of structures that I had demonstrated in my work.
- Reference list looks inspired by my bibliographies. It might be a complete coincidence, but similar to my paper, the References list starts with Dill and ends with Tibbits.
- Many sentences are similar to my past publications. There is an overarching similarity of language that suggests a strong inspiration from my work and words. While I am not going to point out the exhaustive list of all such sentences, I am listing a few here as illustrative sampling:

1. **Authors have used:** “The Skeletide model developed here underlines the most fundamental aspects of protein secondary structure by depicting: (1) the skeletal alpha carbon trace and (2) an accurate representation of long-range intra-main chain H-bonding interactions.”
 - **I had used in my prior work:** “The Peppytide model developed here reproduces several critical aspects of the natural system that impact chain dynamics including the following: (i) dimensional accuracy of bond lengths and bond angles, (ii) a faithful representation of the short-range rotational barrier imposed on all of the backbone dihedral angles, and (iii) long-range stabilization resulting from intrabackbone hydrogen bonding.”
2. **Authors:** “We envision future versions of this model to include attachable side chains that interact with each other and to further tune the relative strengths of interconnects.”
 - **Me:** “An obvious next step is to expand to the full set of amino acid side chains, so that a complete protein tertiary structure can be folded.”
3. **Authors** (a somewhat weaker version): “While this property nicely illustrates the modularity of protein structure—that a single structural unit can be linked together to form a larger, regular secondary structure—it does not accurately mimic the protein folding process in biology.”
 - **Me:** “Although the current Peppytide model is a good tool for studying and teaching polypeptide chain folding, it also illustrates a fundamental architectural principle ubiquitous in biology: that a linear chain of modular units can be configured into a fantastic variety of 3D shapes.”
4. **Authors:** “Therefore, we focus here on dimensionally accurate modular subunits, we call Skeletides, that can (1) link together in predefined geometries using strong magnetic interconnects to create the alpha carbon skeletal backbone and (2) form long-range hydrogen bonds through weaker magnetic interactions. Side chains were omitted to draw attention to the underlying backbone architecture and to simplify construction.”
 - **Me:** “With this vision in mind, we report here the design and fabrication of a tangible, coarse-grained, dimensionally accurate, physical molecular model of the polypeptide chain, which has the necessary degrees of freedom and bond rotational barriers to accurately emulate the backbone folding dynamics of the polypeptide chain.” ... “The long-range hydrogen bond interactions of the polypeptide chain are key to formation of the secondary and tertiary structure. The model reproduces the hydrogen bond donor (NH group) and acceptor (C=O group) behavior of distal amides by using a pair of rod magnets.”

5. **Authors:** “We realized that there is a need for a new, simplified molecular protein model made from modular building blocks (amino acids) that would reveal the most universal, underlying aspects of protein architectures and be simple enough to readily assemble entire protein domains.”
 - **Me:** “There is a strong need for scaled, realistically foldable, but inexpensive, physical models to go hand-in-hand with the AR and other computer interfaces, ... Our approach was to break down the component amino acids into constituent coarse-grained components linked by rotatable bonds. The flexibility of the backbone chain in our model has made it possible to readily build all of the common protein secondary structure elements.”

These are *my* words and my vision that are re-worded and re-used in this paper, that I had developed over the years and hence it has the backstory as I detailed in my blog with a [Peppytide History post](#)¹¹.

Conclusively, the authors have built on top of my work, but they cite my work in a very dismissive, degrading manner in the paper with this sentence: “Peppyptides are another example of a dynamic multicomponent physical model ...”. A proper mention and citation of my work is necessary (Appendix 1).

Conclusion

In conclusion, the authors have thoroughly and exhaustively used my methods, research directions and publications to develop their work and to write the paper. Any mention of that is missing (or intentionally absent). Further, Editor-in-Chief’s action in this matter is decisively absent.

References

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3. Promita Chakraborty. [My funny experience at Berkeley Lab: About a recent publication that is a complete derivative, Part 7](#). Feb 2020.
4. Promita Chakraborty. A Computational Framework for Interacting with Physical Molecular Models of the Polypeptide Chain. 2014. Virginia Tech, PhD dissertation. URI <http://hdl.handle.net/10919/47932>
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11. Promita Chakraborty. [History of Peppyptides, my research journey, and emergence of Physical Scientific Computing](#). Feb 2016.

Appendix 1

Suggestion for annotations to add to the paper is provided here, for the Abstract and Introduction.

1. Annotation suggestion for Abstract

- Adding this to the Abstract:

- “However, it is a challenge to represent all the relevant features of proteins in a single physical model due to their sheer structural complexity. Hence, Chakraborty’s models (Peppytide & PeppyChain) and their expansions into the concepts of a new field of study (Physical Biomodeling) is a pioneering work that shows us how to explore problem solving of this challenge. Here, we have built upon this body of work and made a simplified version where we describe a modular protein model that focuses only on representation of the secondary structure—the underlying structural skeleton.”

- Instead of this:

- “However, it is a challenge to represent all the relevant features of proteins in a single physical model due to their sheer structural complexity. Here, we describe a modular protein model that focuses only on representation of the secondary structure—the underlying structural skeleton.”

2. Annotation suggestion for Introduction

- Adding this note at the beginning of the Introduction:

- “In this paper we are building upon the concepts laid down by Chakraborty’s work on Peppyptides, PeppyChains and Physical Biomodeling that constitute a body of novel work⁴⁻¹⁰, creating a whole new field of study. Chakraborty’s work laid the foundation for how actual physical parameters of scaled, dynamic models for protein folding could be designed, analyzed, and folded into alpha-helix, beta-sheet and beta-turn structures, among other motifs. In this paper, we follow the same path and describe a simplified rendering of polypeptide chains inspired by Peppytide and PeppyChain models, to allow the work to focus on secondary structures of folded proteins, where we are using the same methods and materials for design, computation and analysis.”