Dear Editor Board and Ms. Max Ma,

We recently got the decision of rejection and the 3rd round comments from Reviewer#2. We highly appreciate your encouragement for resubmission.

But given Reviewer#2's comments, we have to make a formal appeal to this decision. By the following arguments, we sincerely wish the board could reconsider our paper.

Section 1: **Point-by-point Response to Reviewer#2's comments at Round 3**

Reviewer#2's comments at Round 3 can be divided into two parts: (1) the claim that Ladderpath approach is not original, and (2) the confusion about the two axes of complexity.

For point (1): The claim that Ladderpath approach is not original

(Reviewer#2's comments marked blue) The central issue of my earlier referee report was that the method developed in Section 2 to analyse the complexity of individual sequences is not original. The LZ compression method was used exactly to this end in the late seventies.

That the two methods are not rigorously identical does not meet the criticism: presenting a mild variant of LZ compression and using it to the same purpose of complexity analysis for individual sequences does not give a new result.

This is a false claim and statement. Ladderpath and Lempel-Ziv compression are distinct in many aspects, and there are lots of new results from our current work:

(i) **Ladderpath and LZ compression give systematically distinct results**, even though we restrict ourselves on strings (which is actually only one application of our Ladderpath approach). We have given the examples in the very first response at Round 1 to Reviewer#2, but we show it here again:

"(quoted from the response at Round 1 to Reviewer#2, marked grey) As the former (Ladderpath approach) outputs a partially ordered multiset and the latter (LZ compression) outputs a compressed string, they are hard to compare directly. Nevertheless, in both algorithms, the final results are actually determined by the calculated scheme of slicing the string, so we can compare their calculated slicing schemes. We use the example string "ABCDBCDBCDCDEFEF" (section 2.2 in the main text): The slicing scheme of the shortest ladderpath (calculated from the algorithm provided) for this string is

"A | BCD | BCD | B | CD | C | D | EF | E | F"

corresponding to the ladderpath Eq (1) in section 2.3 in the main text;

The slicing scheme of the Lempel-Ziv algorithm for the string is

"A | B | C | D | BC | DB | CD | CDE | F | E | F"

We can see that they are different."

In fact, Reviewer#2 has indeed acknowledged this difference by saying that "the two methods are not rigorously identical". But we are not sure why he/she concluded that Ladderpath is a "mild variant" of LZ, because the difference is systematic, no matter the results, the way to calculate, nor the interpretation (even in the narrow case of strings, while Ladderpath can deal with other objects).

(ii) **The definitions of ladderpath-index, order-index, and the nice mathematical properties of**

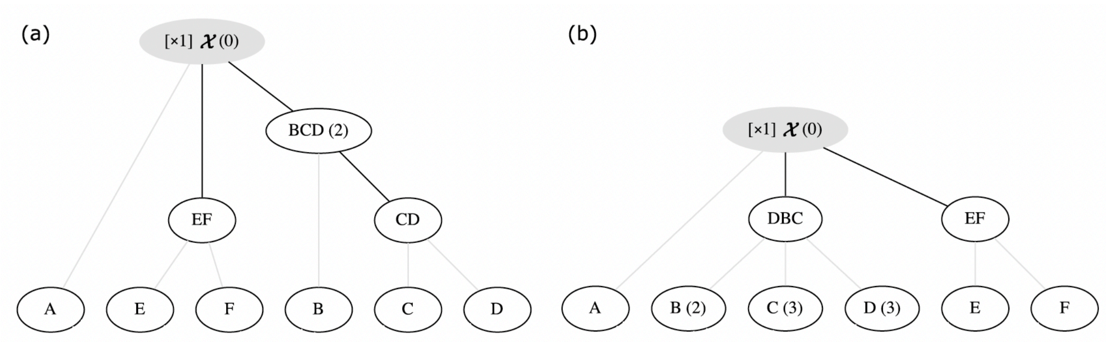
these quantities (e.g., Eq. 3 in section 2.3 and Eq. 6 in section 2.4) **are put forward for the first time**. These concepts and properties are never mentioned in LZ compression, and actually irrelevant with LZ, which are clearly original.

(iii) **Our Ladderpath approach is not only able to deal with strings but also other objects in general** (given the object and its operation-generation can be properly defined); **while LZ compression can only deal with strings** (of course, LZ is efficient and can run on the fly to compress strings, which makes it extremely useful and widely used in data compression. We fully acknowledged that in the Introduction section and the main text, but the point of our paper is not to propose a new algorithm for string compression).

In fact, dealing with strings is only one application of Ladderpath out of many. We chose strings as illustration examples because the string is the simplest case, and easy for the readers to comprehend, since our paper introduced quite a lot of new definitions and concepts.

In fact, besides strings, we also gave a detailed example of 2D patterns (section 2.5, as well as how to calculate its ladderpath in details in Appendix B). Furthermore, we briefly introduced how to deal with chemical molecules (the second half of section 4.3). By all these contents, we intended to give a taste for the potentially diverse applications of Ladderpath, while the main focus of this initial paper is to introduce the basic concepts and definitions.

(iv) Not only the results, the calculating process, and the applicable areas of the two methods are different, **many further concepts can be developed from Ladderpath, which we spent more than half of this paper** (section 3 and 4, as well as section 2.4, 2.5, 2.6) **to discuss, which have never been said or discussed in LZ compression or anywhere else**, e.g., the laddergraph (as shown below, also Figure 1 and 3 in the main text) that explicitly represents the hierarchical relationships among the building blocks (namely ladderons, a new concept defined in our paper) which is the key to understand complexity, the relationships between ladderpath and replication /evolution, how to interpret unknown signals in isolated and non-isolated systems, etc.



The result might be of interest if the new approach were to yield qualitatively new results, compared to the old method. This does not seem likely, however, and the authors do not engage in any such comparisons.

As mentioned, the four points above have clearly shown that there are new results: (i) the outputs are distinct, (ii) the definition of ladderpath-index etc and the derived mathematical properties are never mentioned before, (ii) the applicable areas are different, (iii) further concepts are developed from Ladderpath.

As for the comparisons: To compare the two methods, we can only do that in the case of strings (although Ladderpath has wider applications). And **even so, we did the comparison already in the first response we sent back to Reviewer#2 (grey texts above)**. The difference is systematic.

We did not write those comparisons down in the main text, because the main point of our paper is not to propose a compression algorithm for strings. It may distract the reader from the main storyline, as this paper is already very long and has lots of contents followed. It would be super interesting to have a comprehensive comparison with LZ in the future, in the case of strings.

The authors add that their approach allows to compress structures somewhat more general than strings, such as two-dimensional dot patterns. It would be necessary to look at the literature to find out whether such work has already been done. In any case, however, the extension to dot patterns is not systematically explained, nor does it, in my view, represent a sufficient extension of the LZ algorithm to warrant publication on its own.

First, in fact, **we did review relevant literatures that deal with the "information" of non-string objects** (in the Introduction section), e.g., Francois Jacob's "evolution as tinkering", Knuth's addition chain for integers, Sole's complexity measure for networks/graphs, the molecular assembly trees of chemical molecules in our previous publications. We did stand on the shoulders of giants but there are sufficient differences between Ladderpath and those works, too.

Second, again, **in our view, Ladderpath approach should not be considered as an extension or variant of LZ compression, in any aspect**. Even though we only talk about strings, Ladderpath and LZ compression are distinct, as the reasons given above.

In any case, however, the article spends a considerable amount of time on an algorithm which should be treated altogether by an explicit reference to LZ, saying that the entire approach championed in Section 2 was described there. This would mean a significant reorganisation of the paper, which the authors do not undertake.

First, we did not spend a considerable amount of time on the algorithm; Instead, we spent one subsection 2.7 to discuss the algorithm, while we have 14 subsections/sections in total.

The algorithm is not the main message we intended to deliver, as we have mentioned explicitly in the main text that "the motivation here is to show a proof-of-concept algorithm and code to calculate the shortest ladderpath for a small target or target system". What we intended to deliver are the concepts and definitions of generation-operation, ladderpath, order-index, ladderpath-system, united system, etc. where we used plenty of our ink for.

Second, we are fully aware that LZ is efficient and convenient for the particular purpose of string compression and we acknowledged that in the main text also; Yet, our point is not to provide an efficient and practical compression algorithm.

For point (2): The confusion about the two axes of complexity

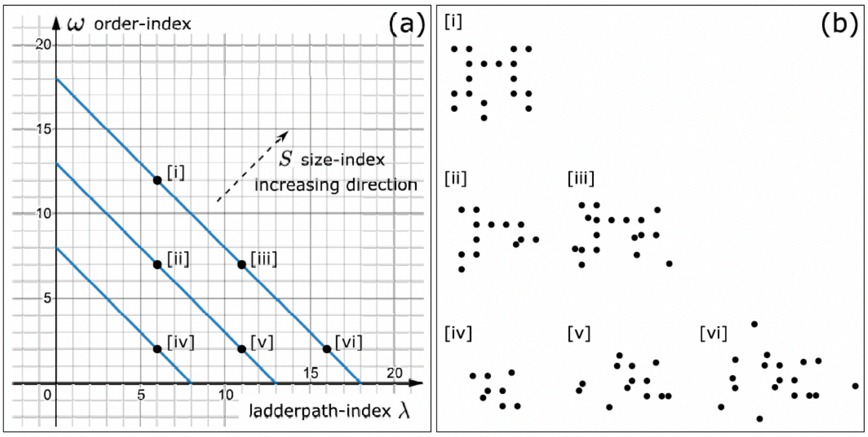
Finally, concerning the ``two axes of complexity'', I still find the authors' views more than a bit puzzling. They say for instance on p.~11: "

It deserves to mention that we may intuitively say that [vi] is more ``complex'' than [i], because the former looks more random/irregular/difficult to reproduce; while we may also say that [i] is more ``complex'' than [vi], because [i] needs more detailed, complex and delicate mechanisms to generate.

However, it is not difficult to realize that these two ``complex" refer to two distinct directions\ldots In fact, the two directions correspond to the ladderpath-index $\lambda$ and the order-index $\omega$, respectively. Therefore, now we are able to distinguish the two axes of ``complexity". ” But [i] and [vi] have the same size, so that λ and ω add up to the same quantity. In other words, any increase in λ yields an equal decrease in ω, and viceversa. In other words, complexity along the ``first axis" is exactly the contrary of complexity along the ``second axis". Simply said, the two axes point in exactly opposite directions. ``Higher complexity" in the first sense of the word is exactly equivalent to ``lower complexity" in the second sense of the word. This is hardly a terminology calculated to bring clarity to a difficult subject.

This statement "the two axes point in exactly opposite direction" is not correct; it happens to be true only in the special case of strings with identical size. In fact, our point is exactly to clarify this concept, which is indeed very hard to grasp as it's never been discussed anywhere else before.

Referring to Figure 2 in the main text (also below), for example, it's easy to show that **both the ladderpath-index and order-index of pattern [iii] are higher than those of [iv], which clearly conflicts with Reviewer#2's criticism** that "the two axes point in exactly opposite direction". For another example, pattern [i] has a higher order-index than that of [iv] while they have the same ladderpath-index, which again conflicts with Reviewer#2's comment. In fact, there are plenty of other examples we can think of, while "point in exactly opposite directions" is only a very special case.



In fact, we have explained this point in the last response, as Reviewer#2 raised the same issue in the last round of comments. It's also because of this misunderstanding, last time he/she suggested that maybe it's more natural to normalize both the ladderpath-index and order-index by the size-index. However, as we replied last time, "(quoted from the response at Round 2, marked grey) they should not be normalized by the size-index S, because the absolute value of the three indices has explicit meanings, for example, larger objects tend to be more "complex" given the same ladderpath-index. If they are normalized, the normalized ladderpath-index of [iv] (6/8=0.75) would be larger than the normalized ladderpath-index of [iii] (11/18=0.61), which does not make much sense and it becomes confusing to interpret the normalized ladderpath-index."

Indeed, Reviewer#2 should not be the person to blame, for missing this point, as it's a new concept and indeed very hard to grasp. Instead, we will add the explanations above into the main text accordingly to make this point clearer.

And finally, I still find it bizarre to compare the complexity of two signals with different sizes, as well as to think of size as being an ``axis of complexity".

As mentioned above, unfortunately Reviewer#2 completely missed the point, and that's why it seems "bizarre" to compare the complexity of two strings with different sizes. Why should we take it as granted that the complexity can only be compared among objects with identical sizes? In fact, we do need a complexity measure among different sized objects.

The size (corresponding to the size-index we defined, roughly speaking) **is a significant factor of the complexity of an object, but it's not simply a proportional relationship** (e.g., not simply the larger the size, the more complex). For example, referring to the figure (b) above, pattern [i] is larger than [v] but [i] is easier to be reproduced (namely, the ladderpath-index of [i] is smaller).

That's exactly why we need two other indices (ladderpath-index and order-index) to clarify this point and represent the two axes of complexity (the three indices are constrained by ladderpath-index + order-index = size-index, but two of them are free).

In my view, the authors have altogether failed to address the core of my remarks which simply states that the bulk of the paper reports results which are not original. The paper should be rejected.

We are confused and have no clue how Reviewer#2's conclusion was made, by simply saying that the bulk of the paper is not original. To summarize, our Ladderpath approach differs from Lempel-Ziv compression in many aspects:

(i) **The results and outputs (including the way to calculate) given by the two methods are systematically different** (we think Reviewer#2 acknowledged this yet his/her claim "the difference is minor" was insisted).

(ii) **Ladderpath applies to many types of objects**. Here we just used strings as examples to illustrate this approach, but also gave examples for 2D patterns in details and for chemical molecules briefly; while LZ only deals with string compression (we think Reviewer#2 acknowledged this).

(iii) **The three indices** (ladderpath-index, order-index and size-index), **as well as their nice mathematical properties, are significant and new concepts** and very useful to clarify complexity, but it's indeed difficult to grasp initially. This part definitely catches Reviewer#2's interests; In the meanwhile, Reviewer#2's criticism for this point is not valid and came from a misunderstanding, which we hope we have fully addressed.

(iv) **Many concepts defined on the basis of Ladderpath have never been said or discussed anywhere else**, including in LZ compression. For example, besides the three indices, there are: the definition of ladderpath-system, how ladderpath connects with replication and evolution (section 3), how to interpret unknown signals in isolated and non-isolated systems (section 4.1 and 4.2), how ladderpath connects to origins of life (section 4.3 and 4.4), etc. which we spent more than half of this paper to discuss.

Section 2: Why we think Reviewer#2's comments are unfair and not unbiased criticisms

Reviewer#2 made valuable comments in the reviewing process, and we revised the manuscripts accordingly, which definitely improved our manuscript. We appreciate his/her time and efforts. However, we think some criticisms are unfair and biased.

First, **many of our responses at previous rounds are simply ignored, and the same claim is repeated without giving sufficient and relevant reasons.**

(i) At Round#1, Reviewer#2 mentioned that the ladderpath "is nothing else than a variation on the LZ compression algorithm proposed in 1978" **yet he/she did not give any reason to support this claim**. In our response at Round#1, we gave detailed reasons why Ladderpath differs from LZ, showed examples how the results given by the two methods are different, and we also revised the manuscript accordingly to make our points clearer.

(ii) At Round#2, **without commenting on our previous response** (about the distinct results given by Ladderpath and LZ), **a slightly different claim was made** that the complexity measure defined in LZ (namely, the quantity $2^{lh_l(u)}$) and in ladderpath are extremely close. **However, this argument and this quantity are not very relevant**, because in Ladderpath approach, the ladderpath itself is the most important while any information measure only reflects some aspect of the ladderpath.

This quantity may be useful to measure the amount of information of infinitely long strings, but infinitely long strings are not our focus (Ladderpath is designed for finite objects, as we explicitly stated in the Introduction), which is actually acknowledged by Reviewer#2 by saying that "true, in order to prove convergence theorems, one needs infinite sequences".

Even so, there would be no conflict that if this quantity is proven to be converging, no matter using LZ compression or Ladderpath approach or other methods (which would be an interesting topic), but this is not the point of our current paper. The detailed explanations are made in our response at Round#2, and Reviwer#2 didn't mention it again in the 3rd round.

(iii) At Round#3, **without commenting on our previous responses** (about the quantity of $2^{lh_l(u)}$), Reviewer#2 simply **repeated to claim that our Ladderpath is not original; But again, he/she didn't give any extra reason** but just said that we didn't fully illustrate how our Ladderpath approach can be applied to 2D patterns and other objects. In this response, we explained in details why we used strings as the example to illustrate our approach, and in fact, we have already illustrated 2D patterns in details and chemical molecules briefly in the manuscript.

We think it's absolutely unfair to simply ignore our previous responses and repeat the same claim without giving sufficient and relevant reasons. We think we have fully addressed Reviewer#2's concern about originality. **Without commenting on our responses (by just ignoring them) or providing reasonable arguments further, we think this criticism of originality should not be used as one of the two main reasons to reject our paper.**

Second, the issues about the "two axes of complexity" was also raised in every round. But yes, these are appropriate arguments and discussions where he/she didn't ignore our responses (and we appreciated that). However, with two rounds of explanations, there was unfortunately still confusion, which made Reviewer#2 wrongly concluded at Round#3 that "the two axes point in exactly opposite directions".

We explained it in details in this document above why this criticism is false (he/she treated a special case as a general case). We will add extra sentences in the main text to make this point even clearer. But **<u>we think this misunderstanding of Reviewer#2 should not be used as another one of the two main reasons to reject our paper.</u>**

Third, **<u>our paper has 25 pages</u>** (in the journal's format, without references), 14 subsections/sections, and 4 appendix sections, but Reviewer#2 only commented on the very first half and **<u>ignored all the rest</u>** (he/she indeed briefly commented on subsection 4.4 at Round#1, but after our response, he/she didn't comment further or raise any question again).

<u>This is unfair and inappropriate</u>, and we wonder why. In fact, Reviewer#2 showed much interests for the latter part of our paper, by saying at Round#1 that "the general considerations which end the paper appear to be of significant interest".

Lastly, Reviewer#2 **<u>changed his category scores for our manuscript back and forth, while the parts we revised in the main text has no chance to affect these scores.</u>** These changes seemed very subjective and arbitrary, and made us wonder why.

Referring the screenshots below, both "Are the methods adequately described?" and "Are the conclusions supported by the results" are changed from "Yes", to "Not applicable", and back to "Yes", but we actually didn't revise either the methods part or the results part (we just added and revised explanatory texts).

We are happy to see that "Are all the cited references relevant to the research?" are changed from "blank" to "Yes", although Reviewer#2 still saying that we should investigate if there're literatures that deal with objects other than strings (which we have already done, as explained above).

Round#1	Yes	Can be improved	Must be improved	Not applicable
Does the introduction provide sufficient background and include all relevant references?	( )	( )	(x)	( )
Are all the cited references relevant to the research?	( )	( )	( )	( )
Is the research design appropriate?	( )	( )	( )	(x)
Are the methods adequately described?	(x)	( )	( )	( )
Are the results clearly presented?	(x)	( )	( )	( )
Are the conclusions supported by the results?	(x)	( )	( )	( )

Round#2	Yes	Can be improved	Must be improved	Not applicable
Does the introduction provide sufficient background and include all relevant references?	( )	( )	(x)	( )
Are all the cited references relevant to the research?	(x)	( )	( )	( )
Is the research design appropriate?	( )	( )	( )	(x)
Are the methods adequately described?	( )	( )	( )	(x)
Are the results clearly presented?	(x)	( )	( )	( )
Are the conclusions supported by the results?	( )	( )	( )	(x)

Round#3	Yes	Can be improved	Must be improved	Not applicable
Does the introduction provide sufficient background and include all relevant references?	( )	( )	(x)	( )
Are all the cited references relevant to the research?	(x)	( )	( )	( )
Is the research design appropriate?	( )	( )	( )	(x)
Are the methods adequately described?	(x)	( )	( )	( )
Are the results clearly presented?	(x)	( )	( )	( )
Are the conclusions supported by the results?	(x)	( )	( )	( )

Finally,

We want to bring Reviewer#1's comments back. He/she gave very positive feedbacks from the beginning, and acknowledged the novelty of our work, by saying that (quoted):

"This is especially important when proposing something new. As we know, **it is very difficult to break through with new topics**." (through revision where we added texts and citations accordingly to make this point clearer, we believed that Reviewer#1 is content)

"**This article is not easy to read. However, I would not take this as an objection. It requires increased attention.** Moreover, the authors made sure that the reader had the best possible ease."

"In my opinion, **the article is worth publishing**."

Given the arguments above, we sincerely wish the board could reconsider our paper.
But no matter what the final conclusion is, we sincerely appreciate your time.
Thank you very much,

Regards,
Yu Liu and co-authors