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By this letter, I am alerting the scientist community of the misbehavior of Pr Lev S. Tsimring acting under the umbrella of a Division editor at PRL. After our manuscript was refused to be sent for evaluation by experts, based on no argumentation by an assistant editor, with no much competence in the field of stochastic process in cell biology, Pr Lev S. Tsimring tried to confirm this unfair decision, by an apparent aggressive review, full of mistakes, wrong statements, claiming that most of our "statements [in our manuscript] are likely to be wrong". This is a clear case of defamation and this behavior is simply unacceptable, because actually, our statement are actually correct and proved either by analysis, simulations and confirmed by the recent publication of this article

M Dora, D Holcman

Active flow network generates molecular transport by packets: case of the endoplasmic reticulum

Proceedings of the Royal Society B 287 (1930), 20200493

Although I have simply demanded that our manuscript be sent to expert to a fair evaluation, based on Pr Lev S. Tsimring unprofessional letter, ignoring the scientific standard and rigor, the following response questions his ability to serve as a Division editor of PRL

Paper: https://arxiv.org/abs/1810.07272

COMMENT:
Comment to host review: I concur with the initial editorial decision to reject the manuscript in question without review.While the active unidirectional switching network is indeed unusual, and the numerical observations of the active transport of molecules on this network reveal certain interesting properties, the results are not truly surprising.
ANSWER: from this comment, I am not sure that Pr Lsmiring has read carefully our manuscript: contrary to what he said, active unidirectional flow is not" a numerical observation": this is a fact from experiments (Nature Cell Biology, 2018.) In addition, it is not clear which interesting property he is talking about. The statement likes precision.

COMMENT: Of course if the flow direction is switching sufficiently slowly, there will be accumulation of particles in the "capture nodes" where all three edges point inward, and once the low direction in one of the edges reverses, there will be a large outflow from that site (a packet, in authors' terminology).
ANSWER: I am afraid that this statement is incorrect: contrary to what Pr Lsmiring said, there are no accumulation of particles in capture nodes. First, nodes capture particles transiently, so it is a time dependent process. Second the nodes do not accumulate particles.

COMMENT:It is peculiar that the MFPT has a minimum at a certain mean switching time, but it is just an empirical observation without any attempt to understand why it is happening, and find the MFPT theoretically for this model.
ANSWER: This statement is also misleading, suggesting at this time that Pt Lsmiring has not read carefully our manuscript until this end: we indeed do have the analytical explanation for the minimum using the return probability that we computed using Markov process approximation.

COMMENT:
While the paper claims that this minimum time "is compatible" with
experimental observations in ER, in fact it differs by at least one
order of magnitude (0.2s vs 4s).
ANSWER: this statement is also incorrect and the quotation of magnitude are erroneous: We have exactly explored the range suggested in our previous manuscript published in Nature Cell Biology, 2018 where we have specifically recall that the range is between 30 ms to 3s and not 0,2 to 4s, as stated here.

COMMENT:
The comparison between this new network transport model and "classical" diffusive transport models is rather superficial and also hard to access given that the model was not introduced clearly
ANSWER: This statement about clarity is revealing that Pr Lsmiring has not understood our model, which is confirm by the next comments.

COMMENT:
what is assumed for the particle hopping between the nodes (random Poisson process, deterministic flow, something else?), is not specified.
ANSWER: the motion of particles described as Poissonnian in network is classical in the field. We recall that the flow direction only allows to accept whether a transition between neighboring nodes could be made or not.

COMMENT:
Some conclusions of the manuscript are not supported by the data.
ANSWER: Pr Lsmiring is talking about comparison between our results and data here. This is surprising because we do not have presented any data in the manuscript. Data were actually previous published in the Nature Cell biology paper, from which our manuscript was built upon. Actually this statement that our manuscript is not supported by data does

not make sentence and actually we have now new experimental data to support our new prediction, which is the goal of our next paper.

COMMENT:For example, the statement that in classical diffusive models particles are distributed uniformly among the nodes, and in this model they are not, is likely wrong.

ANSWER: The use of terminology "likely wrong" is surprising in science: either PR Lsmiring makes a statement that our results are wrong and then it should give a proof or if he is not sure about what he is not talking about, he should probably not make the statement at all.
In the present case, PR Lsmiring is again making a wrong statement. It is extremely classical that the steady-state distribution of a diffusion process is given by the first eigenfunction, which is a constant in a bounded domain. Here in the quasi-steady state, this is not the case, as we have shown numerically and give an analytical argument in the end.

COMMENT:
If we are talking about long-term average, then in both cases the distribution will be uniform. Instantaneous distributions are non-uniform in both cases.
ANSWER: This is another wrong statement of PR Lsmiring. We have started to explain the phenomena analytically toward the end of the paper. The main difference between diffusion and active network is the correlation of the nodes.

COMMENT: The magnitude of fluctuations in each node will probably be different, but this was not addressed in the paper.
ANSWER: This is another incorrect statement: we described the two time scales for the node and the flow.

COMMENT:The statement that only in the directional model the fastest particles travel along the shortest paths, is also probably wrong.
ANSWER: we do not make such a statement. We actually said that the shortest paths are quite similar but not exactly equal. This effect is subtle and claiming that this statement is " probably wrong" is quite unprofessional.

COMMENT:In standard random walk models the fastest particle among many is also the one that chooses the shortest path.
ANSWER: This statement shows that PR Lsmiring is not aware of our recent discoveries summarized in our recent review: Z Schuss, K Basnayake, D Holcman, Redundancy principle and the role of extreme statistics in molecular and cellular biology, Physics of life reviews 2019

COMMENT: Generally, the manuscript suffers from the lack of in-depth analysis that goes beyond straightforward numerical simulations. Papers that are deemed suitable for publication in Physical Review Letters are expected to have that kind of serious analysis in them.

ANSWER: **The conclusion of Pr Lsmiring is not supported by his collection of incorrect and misleading statements. This is clearly an unacceptable attitude for a divisional editor at PRL whom should probably resign his position.**