Comments to the Author,

This paper develops and illustrates a novel approach to detect the threshold points for the gene expressions. To apply this strategy, three methods and their corresponding algorithms are proposed which are utilizing Hotelling's T2, T2 statistic and empirical distribution for the sample first-order and second-order derivatives. Both the motivation and the strategy as well the method proposed are well illustrated. However, several small problems should be considered to make the manuscript acceptable by Statistics and Its Interface. In general, I would recommend acceptance if the authors can address my concerns as the following,

1, The authors provided the pseudocode in the manuscript, however, it would deeply limit the usage and citation of the current works. The preliminary R script (Bioconductor or Github) or Matlab script should be provided so that the reader could be used not only by statistic but also biologists and clinicians.

2, As author mentioned in the Discussion section, the current proposed method could extent to multiple threshold, actually, the real-biological metabolism is exactly as the multiple homeostasis, I prefer the multiple threshold would be more common than single threshold homeostasis.

3, The idea mentioned by present study that gene cluster and classification by threshold time were quite novel. It would be a great motivation to apply current method in this context and try to find some interesting biological discoveries. If the author could find such kinds of data, I encourage the authors make a try or else they can provide some preliminary event why the author have such hypothesis.