

Dear Editor:

On behalf of all coauthors, I like to thank you and all reviewers for the very careful and critical review of our manuscript. Indeed, these critical comments helped us to further improve the quality of this manuscript. We thoroughly addressed all the concerns raised by the reviewers, these modifications were labelled with red in the re-submitted manuscript.

Here below are the changes we made on this manuscript in response to the reviewers' comments given point by point.

Reviewer 1

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: 1. Figure title should be concise 2. Provide the equation numbers 3. The main problems of the paper are: lack of comparisons with the results of previous researchers, unclear formulation of the algorithm, unclear scheme for validating the results.

1. The reviewer's comment: Figure title should be concise.

Response: Thanks for your kindly suggestion. We have reconsidered and modified the title of all the three figures in our manuscript. The modifications of these titles were list as follows:

Figure number	Original title	Revised title
1	Diagram of the electrophoresis-based	Diagram of the classical electrophoresis-based

	immunoassay microfluidic chip for the real-time islet insulin detection and the operating principles in the key channel.	immunoassay microfluidic chip
2	Theory of fluorescence anisotropy-based insulin concentrations sensing technique.	Theory of fluorescence anisotropy-based insulin sensing
3	Theory, optical path and real-world system of LSPR based islet secretome sensing technique.	LSPR based islet secretome sensing

2. The reviewer's comment: Provide the equation numbers

Response: We apologize for this mistake. We have added the equation number at the right side of the equation line as you suggested.

3. The reviewer's comment: The main problems of the paper are: lack of comparisons with the results of previous researchers, unclear formulation of the algorithm, unclear scheme for validating the results.

Response: Thanks for your detailed comments. Because this is a review, so we have no Results section. We demonstrated in this manuscript are merely the marvelous designing of three independent microfluidic chips applied in islet secretome area. Besides, the focuses of this review are main on the theory, applications, advantages and disadvantages of these chips. Thus, we have no comparisons or validating results sections in our manuscript.

For the formulation problem, we are grateful for your comments, we carefully read the paragraphs containing algorithms, we revised the formulation to make it more readable and understandable, and we also cited the original article that containing the detailed derivation procedure for the algorithm in revised manuscript.

Reviewer 2

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Diabetes mellitus is a global health disease that results from islet dysfunction or insulin resistance. The mechanisms of islet dysfunction are still under exploration. Islet hormone secretion as the main function of the islet plays an important role in the homeostasis of blood glucose. Explaining the detailed mechanism of islet hormone secretome distortion can provide clues to treating diabetes. Therefore, it is crucial to develop accurate, real-time, labor-saving, high-throughput, automated, and cost-effective techniques for the detection of islet secretome. Microfluidic chips, an elegant platform with a combination of biology, engineering, computer science, and biomaterial, have attracted tremendous interest from scientists in diabetes all around the world. These tiny devices are miniatures of traditional experimental systems with more advantages of time-saving, reagent-minimization, automation, highthroughput, and online detection. These features of microfluidic chips meet the demands of islet secretome analysis, and varieties of chips have been designed in recent 20 years. In this review, a brief introduction to microfluidic chips is described, and three microfluidic chips-based islet hormone sensing techniques are summarized. We focus mainly on the theory of these techniques and then give detailed examples based on these theories. We hope to provide some insight into the design of future chips and

detection systems. In General: it's a good paper and the subject of the manuscript is applicable and useful. Title: the title properly explains the purpose and objective of the article Abstract: abstract contains an appropriate summary for the article, the language used in the abstract is easy to read and understand, and there are no suggestions for improvement. Introduction: authors do provide adequate background on the topic and reason for this article and describe what the authors hoped to achieve. Results: the results are presented clearly, the authors provide accurate research results, and there is sufficient evidence for each result. Conclusion: in general: Good and the research provides sample data for the authors to make their conclusion. Grammar: Need More revision. (Check The Paper Comments). Please provide the following information in the Paper 1. Conflict of Interest 2. Source of Funding Finally, this was an appealing article, in its current state it adds much new insightful information to the field.

1. The reviewer's comment: Grammar: Need More revision. (Check The Paper Comments).

Response: We apologized for the written. We carefully read the manuscript and made some revises for language. We also performed a language polishing by a professional English language editing company. The language certificate is uploaded as an attachment.

2. The reviewer's comment: Please provide the following information in the Paper 1. Conflict of Interest 2. Source of Funding

Response: We are grateful for the thoughtful reminder of the reviewer. The conflict of interest forms by all authors were uploaded as attachments to the submission system. The source of funding was included in the Funding section.

Revision reviewer's comments: Accept

Response: Thanks for your comments

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) *Science editor:*

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thanks for the assessment of science editor.

(2) *Company editor-in-chief:*

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is

'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thanks to the chief editor's comments, we carried out the corresponding revises according to these comments.