

## **Label-free graphene-based impedimetric biosensor for real-time tracing of the cytokine storm in blood serum; suitable for screening COVID-19 patients**

Mohammad Ali Khayamian<sup>1,2,3,\*</sup>, Mohammad Salemizadeh Parizi<sup>1,2</sup>, Mohammad Reza Ghaderinia<sup>1,2</sup>, Hamed Abadijoo<sup>1,2</sup>, Shohreh Vanaei<sup>1,2,4</sup>, Hossein Simaee<sup>1,2,6</sup>, Saeed Abdolhosseini<sup>1,2</sup>, Shahriar Shalileh<sup>1,2</sup>, Mahsa Faramarzpour<sup>1,2</sup>, Vahid Fadaei Naeini<sup>3,5</sup>, Parisa Hoseinpour<sup>7</sup>, Fatemeh Shojaeian<sup>8</sup>, Fereshteh Abbasvandi<sup>9</sup>, Mohammad Abdolahad<sup>1,2,10,\*</sup>

<sup>1</sup>Nano Electronic Center of Excellence, Nano Bio Electronic Devices Lab, School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran, P.O. Box 14395/515

<sup>2</sup>Nano Electronic Center of Excellence, Thin Film and Nano Electronics Lab, School of Electrical and Computer Engineering, University of Tehran, Tehran, Iran, P.O. Box 14395/515

<sup>3</sup>School of Mechanical Engineering, College of Engineering, University of Tehran, Tehran 11155-4563, Iran

<sup>4</sup>School of Biology, College of Science, University of Tehran, P.O. Box: 14155-6655, Tehran, Iran

<sup>5</sup>Division of Machine Elements, Luleå University of Technology, Luleå, SE-97187, Sweden

<sup>6</sup>Integrative oncology department, breast cancer research center, Motamed Cancer Institute, ACECR, Tehran, Iran

<sup>7</sup>SEPAS pathology Lab, Tehran, Iran, P.O.BOX 1991945391

<sup>8</sup>Imam Hossein Clinical Research Development Center, Imam Hossein Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran

<sup>9</sup>ATMP Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, P.O. BOX 15179/64311, Tehran, Iran

<sup>10</sup>Cancer Institute, Imam-Khomeini Hospital, Tehran University of Medical Sciences, P.O. BOX 13145-158, Tehran, Iran

\*Corresponding authors: [m.abdolahad@ut.ac.ir](mailto:m.abdolahad@ut.ac.ir), [abdolahad@tums.ac.ir](mailto:abdolahad@tums.ac.ir), [m.a.khayamian@ut.ac.ir](mailto:m.a.khayamian@ut.ac.ir), [m.a.khayamian@gmail.com](mailto:m.a.khayamian@gmail.com)



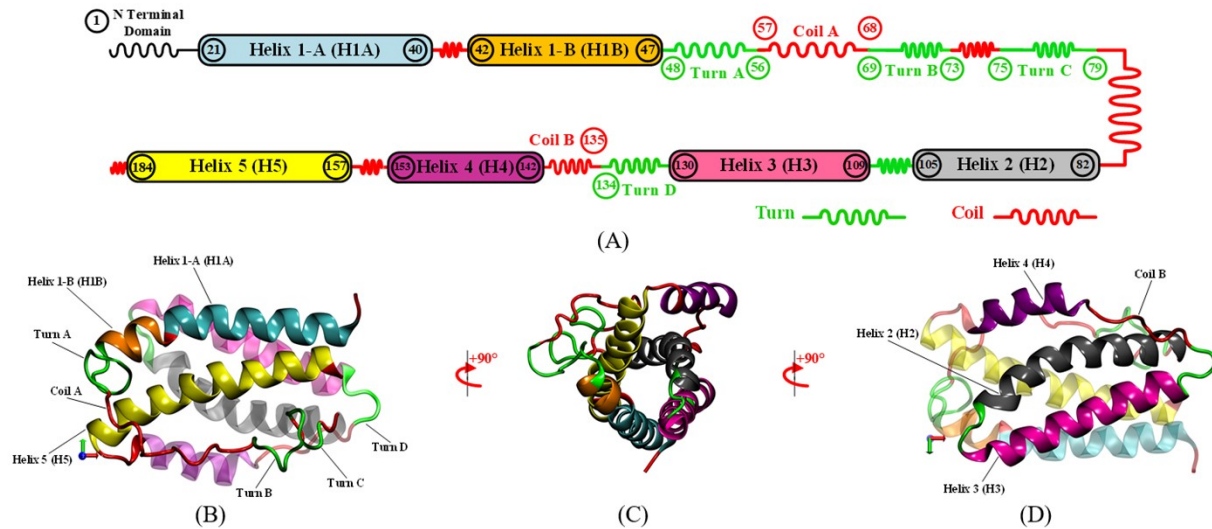


Figure S3 (A) Schematic representation of Interleukin 6 (IL-6). The range of residue numbers is given for each domain at its beginning and end. New cartoon representations of the IL-6 fold representing the four membrane helices (Transparent yellow, Transparent pink, Transparent purple, Transparent gray), and the two malformed helices (Cyan and Orange) as well as the connecting loops including coil and turn domains. (B) Left side view; (C) End-on view; (D) Right side view.

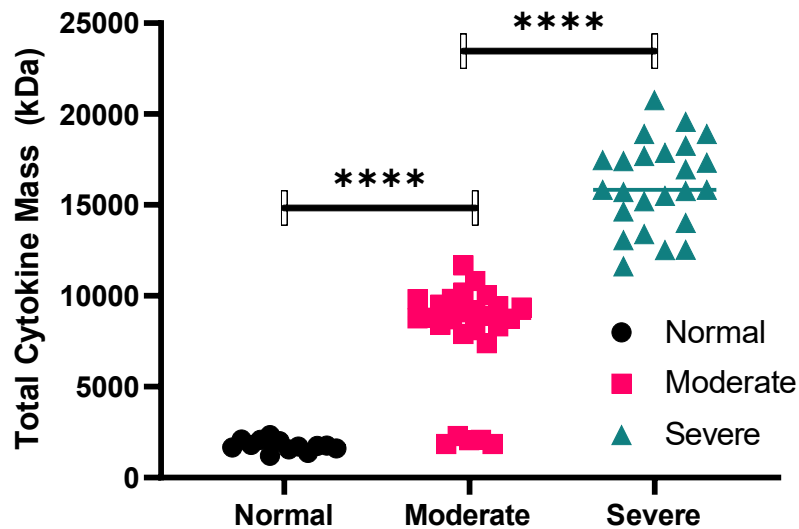


Figure S4 Comparing secreted levels of total cytokine mass in the blood serum of normal donors, and patients with moderate and severe hypercytokinemia. Here, hypercytokinemia alone means sum of the moderate and severe cases. The total cytokine mass was measured by ELISA for all of the 63 samples.

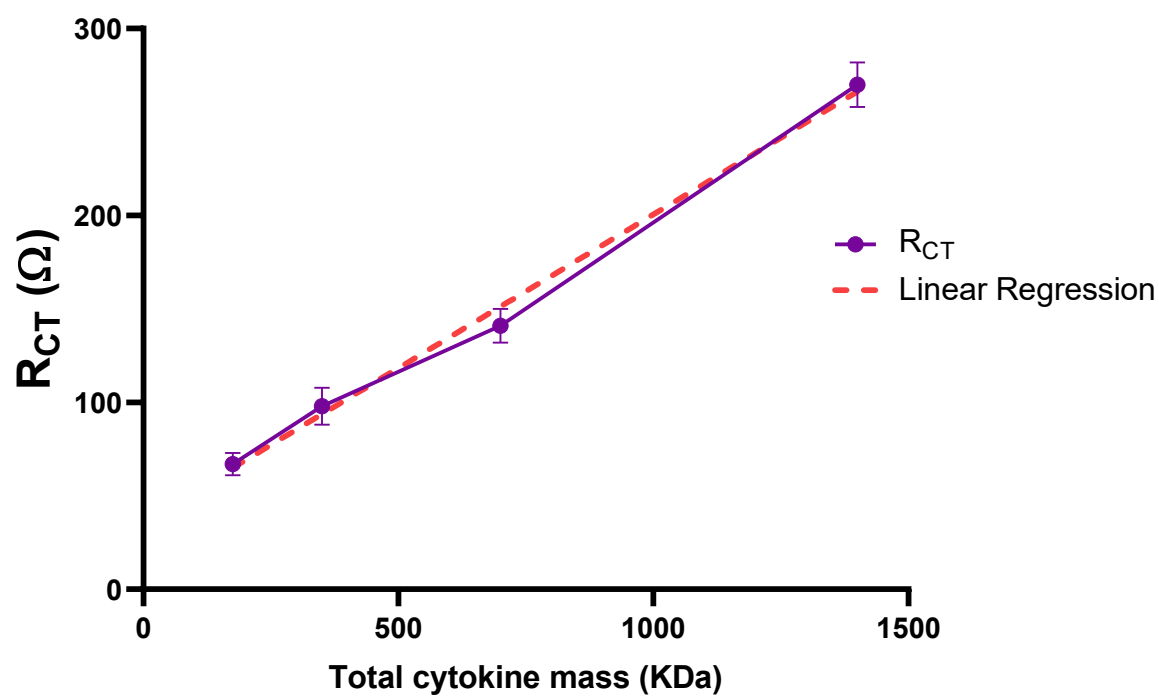


Figure S5 Electrochemical response studies of developed EIS-biosensor for blood serums with a specified amount of total cytokine mass, which is almost a linear function. The detection limit for the device is calculated as 175 kDa total cytokine mass.

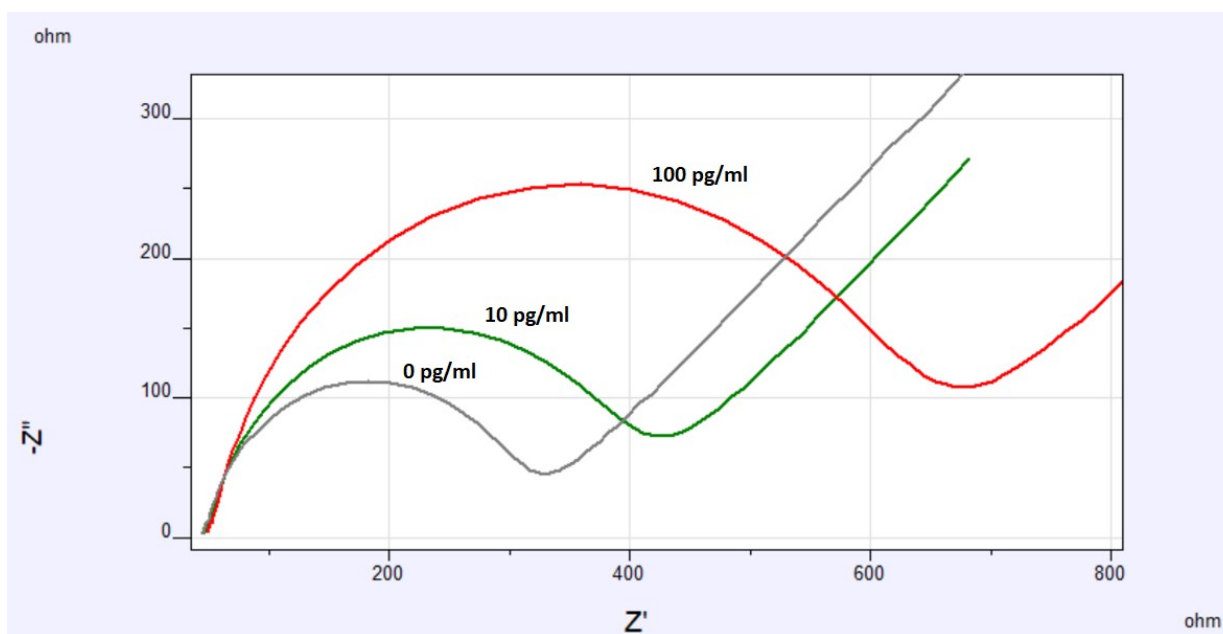


Figure S6 The EIS analysis was done and the Nyquist diagram was plotted for different concentrations of the IL-6 in a human serum.

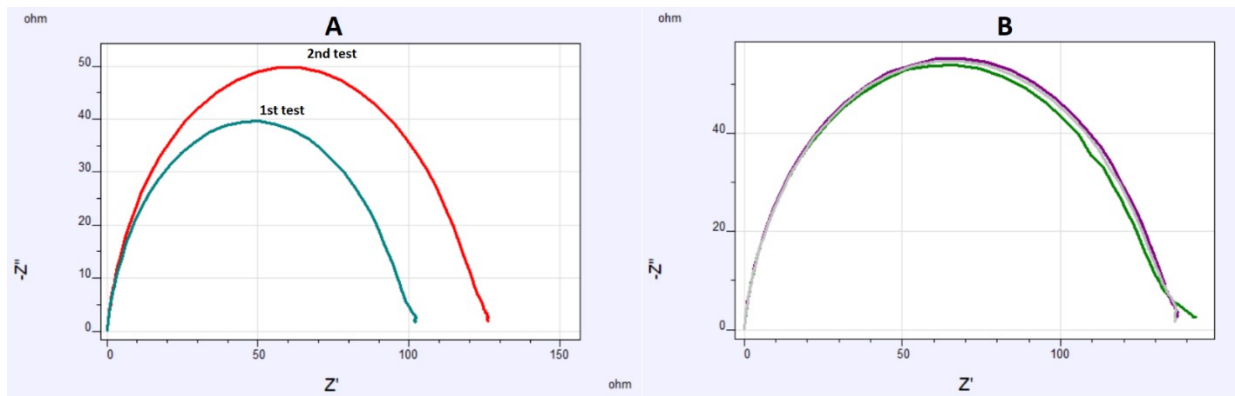


Figure S7 (A)  $R_{CT}$  analysis from the blood serum of a healthy donor for two consecutive experiments and after each time of exposing to graphene/cu electrode. (B) the EIS results of a blood serum tested on three different sensors with a new graphene electrode.