Development and characterization of a novel Barrier-on-chip including dual fluidic chambers and integrated TEER electrodes

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Introduction **:** *Cell barrier integrity is crucial for proper regulation of molecule and ion movement between different tissues. Understanding mechanisms leading to barrier dysfunction in diseases, such as gastrointestinal and neurological disorders, is essential for the development of new therapies [1,2]. Microphysiological systems (MPS) are currently used to reproduce cell barriers in vitro to study cell physiology, barrier function and drug testing in healthy and disease conditions. Common cell barrier monitoring approaches such as imaging techniques involving immunostaining tight junctions, and bio-impedance measurement, particularly impedance measurement at different frequencies to monitor the cells' Transendothelial/epithelial Electrical Resistance (TEER), are used to assess cell barrier integrity.*

Our laboratory has developed an advanced, cost-effective MPS to measure TEER in a Barrier-on-Chip model with integrated microfabricated electrodes using an in-house developed impedance measurement device (TEEROC) [3]. Additionally, the transparency and fluidic properties of the developed MPS allow structural assessment of tight junctions by immunofluorescence imaging.

Biology and Technology **:** *The developed MPS contains two fluidic chambers separated by a porous membrane, which enable co-culture of endothelial or epithelial cells together with tissue-specific cell types thereby allowing the establishment of different in vitro tissue models. Furthermore, a pump system can be connected to the MPS via standardised luer connectors for culturing cells under dynamic conditions. Validation of biocompatibility, TEER measurement capability and usability for immunofluorescence was performed using intestinal Caco2 cells.*

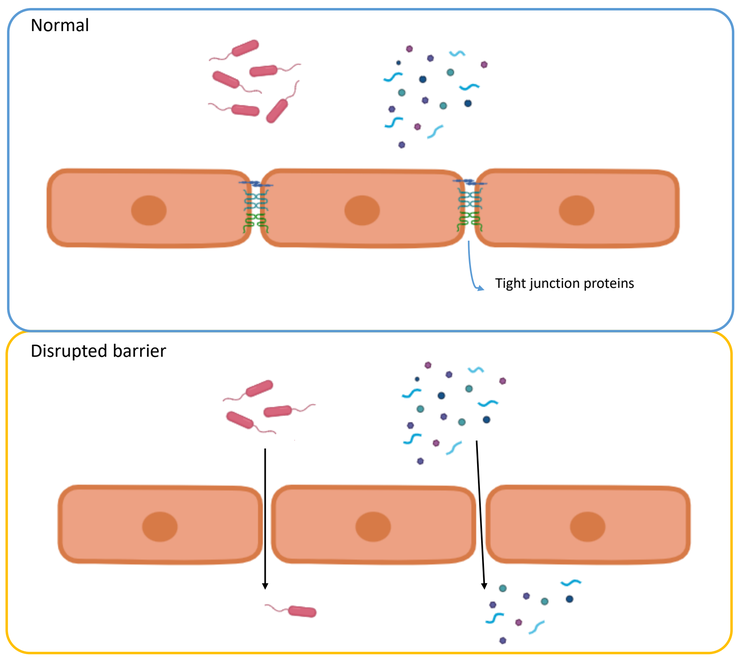

Figure 1 – Cell barrier function is maintained by a series of tight junction proteins. Tight junction proteins connect adjacent cells and prevent pathogens and protein from traversing the paracellular space.

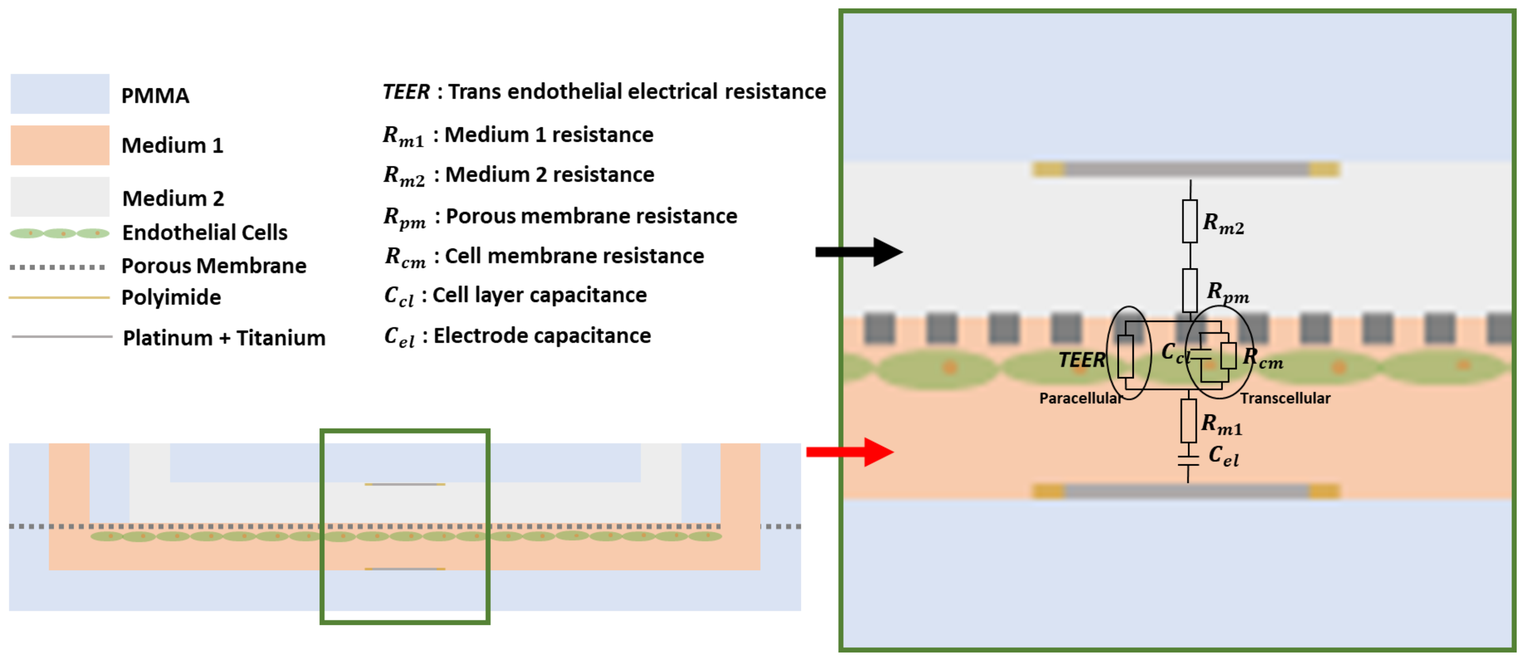

Figure 2 - Detailed equivalent electrical circuit for TEER measurement within a two-channel MPS. The black arrow designates the basal chamber, and the red arrow designates the apical chamber of the MPS.

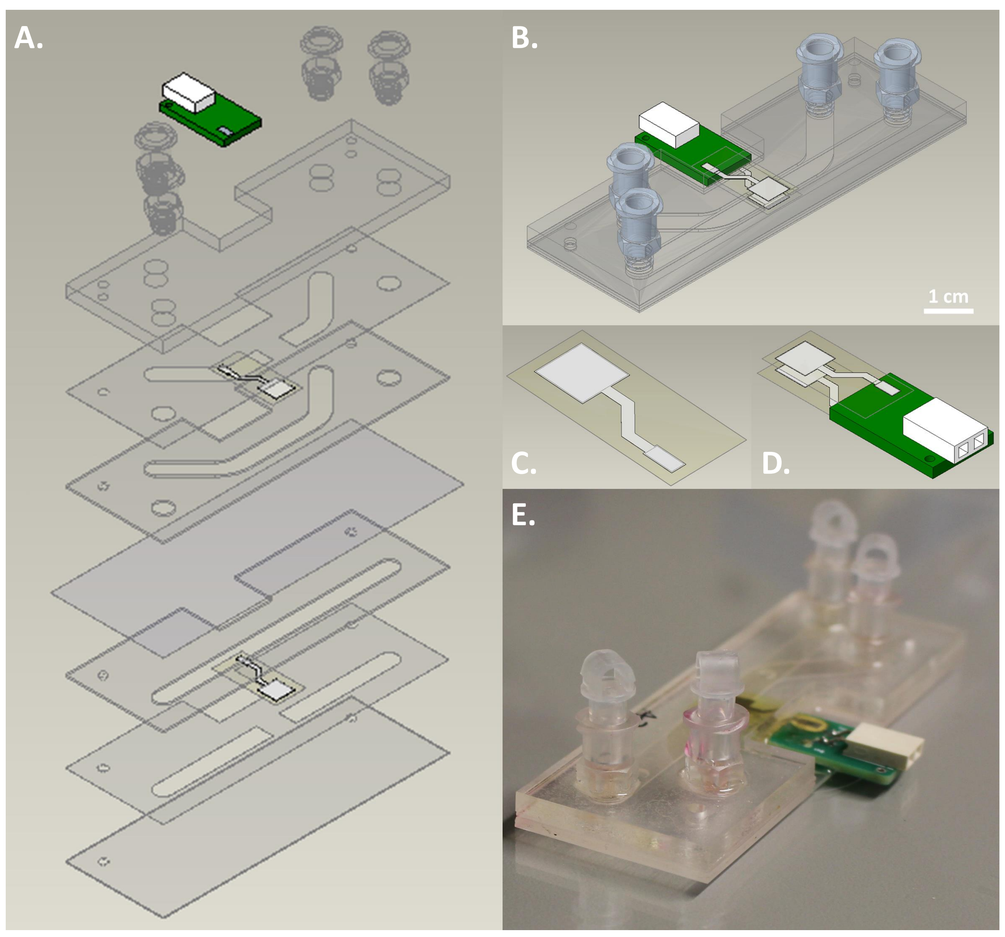

Figure 3 – Microphysiological system prototype. (A) Exploded view of the MPS composed of PMMA sheets, double-sided transparent tape, porous PET membrane, two electrodes, one PCB, and four female luers. (B) Isometric view of the MPS. (C) Isometric view of the electrodes CAD. (D) Isometric view of the mounted PCB with the connector to the impedance recording device and the electrodes in white. (E) The built device with Caco2 cells and a medium inside.

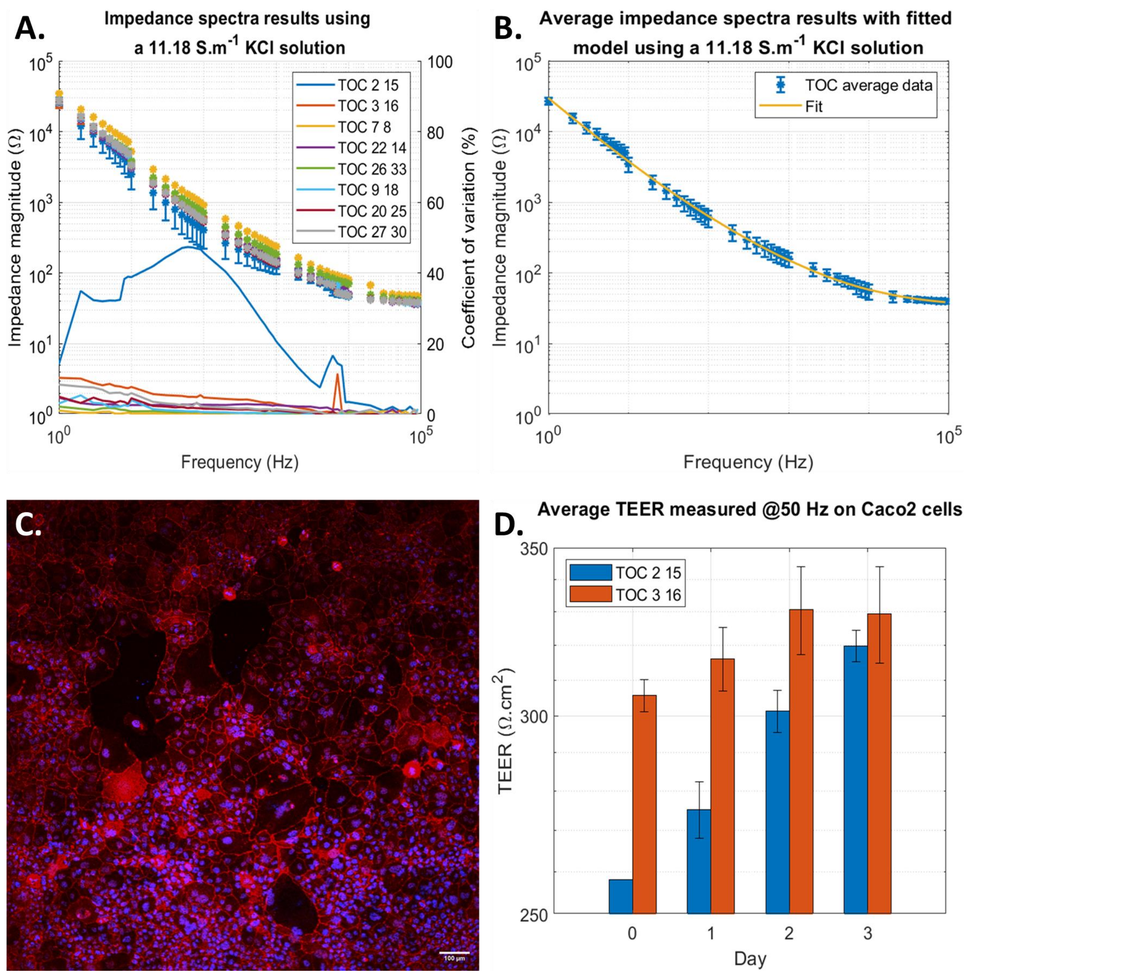

Figure 4 – Characterisation using KCl conductive solution and biological experimentation. (A) Impedance magnitude function of the frequency for eight different MPSs (dots). Curve represents the coefficient of variation in functions of the frequency. (B) Average impedance magnitude value of the eight MPSs. (C) Fluorescent imaging results of the Caco2 cells. The nuclei are shown in blue using DAPI, and the tight junctions are shown in red using ZO-1. (D) Average value measured for the Caco2 cells at 50 Hz during the first culturing days.

Conclusions **:** *HEPIA has built an advanced, cost-effective MPS to measure TEER in a Barrier-on-Chip model. The advanced electrode design and compact PCB integration significantly enhances TEER measurement accuracy. Its versatile PMMA structure and electrode designs allow rapid customisation for different biological barriers, paving the way for broader tissue engineering and biomedical research applications. Future work will focus on optimising the device for diverse cell types and drug testing.*

References

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