

Blood Brain Barrier: A Selective Porous Graphene Membrane-based molecular Communications Channel

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Introduction

The rapidly growing field of cerebrovascular research has created exciting opportunities where reproducing the BBB in vitro represents a critical biotechnological breakthrough. This is because it would allow scientists to understand the cerebrovascular response to a number of physiological stimuli and create a more streamlined process to find potential cures[1].

It has been recognized that mimicking the in vitro response of the BBB is an incredibly challenging task as seen by the various mechanisms of passage seen in Fig. 1. A potential solution to overcoming the challenges of in vitro testbeds is with the use of nanoporous graphene membranes. As a first step, this could be through the creation of a structure that inhibits the passage of large molecules whilst enabling the passage of water, glucose as well as small monomers such as amino acids. The aim of this project was to fabricate a porous graphene membrane which can allow selective passage based upon molecular size behaving essentially as a molecular sieve. It should especially be fully permeable to water molecules.

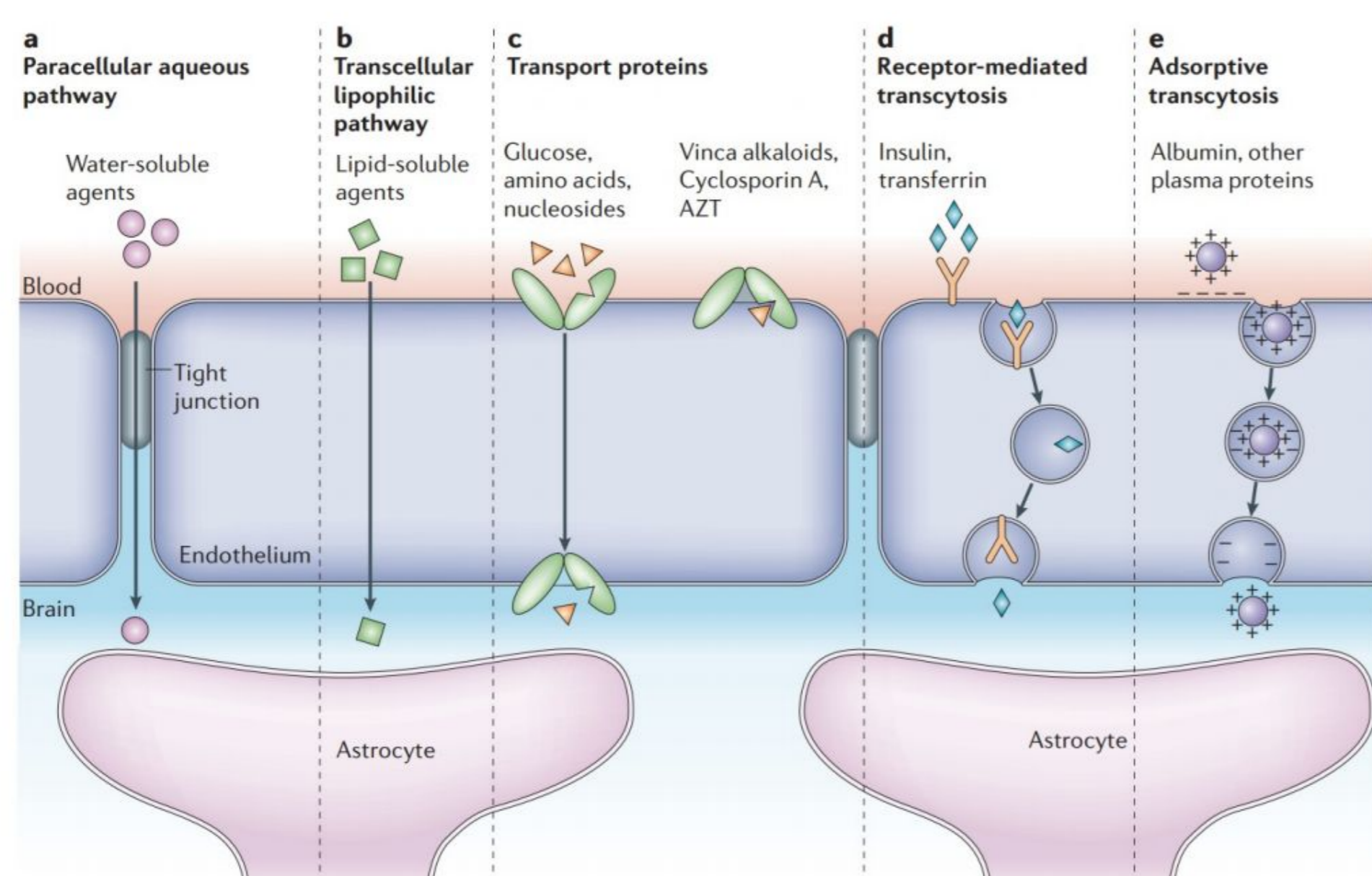


Fig.1: Pathways across the Blood Brain Barrier: A Schematic diagram of the endothelial cells that form the blood-brain barrier (BBB) and their associations with the perivascular endfeet of astrocytes [2]

Experimental Methods

Fabrication of Graphene

Graphene was fabricated on a copper substrate using chemical vapour deposition. A standard graphene wet transfer was subsequently used that resulted in the graphene being deposited on silicon substrate. These initial samples were characterized using Raman spectroscopy.

Fabrication of nanoporous graphene

Nanopores were produced on the graphene through reactive ion etching using Argon gas. The power and time of the reactive ion etching was varied across 6 samples that were used.

Characterization of the nanoporous graphene

The nanoporous graphene fabricated was characterised using Raman spectroscopy at wavelengths of 457nm, 514nm and 633nm which would allow for the determination of the defect density to be attained. Atomic force microscopy and scanning electron microscopy were used for further characterization.

References

- [1] PICHLER, A., KHALIL, M., LANGKAMMER, C., PINTER, D., BACHMAIER, G., ROPELE, S., FUCHS, S., ENZINGER, C., AND FAZEKAS, F. Combined analysis of global and compartmental brain volume changes in early multiple sclerosis in clinical practice. *Multiple Sclerosis* (2015).
- [2] ABBOTT, N. J., AND ROMERO, I. A. Transporting therapeutics across the blood-brain barrier, 1996.
- [3] SURWADE, S. P., SMIRNOV, S. N., VLASSIOUK, I. V., UNOCIC, R. R., VEITH, G. M., DAI, S., AND MAHURIN, S. M. Water desalination using nanoporous single layer graphene. *Nature Nanotechnology* (2015).

Results

Raman Spectroscopy

Some of the samples Raman spectra taken at 514nm that were taken can be observed in Fig. 2 where it is shown that increasing etching time and etching power resulted in a clear increase in defect density shown by the increasingly prevalent D-peak and the reduction in the intensity of the 2D-peak. Table 1 shows the inter-defect density attained for the different samples which further corroborates these findings as increasing power/time results in lower inter-defect distances.

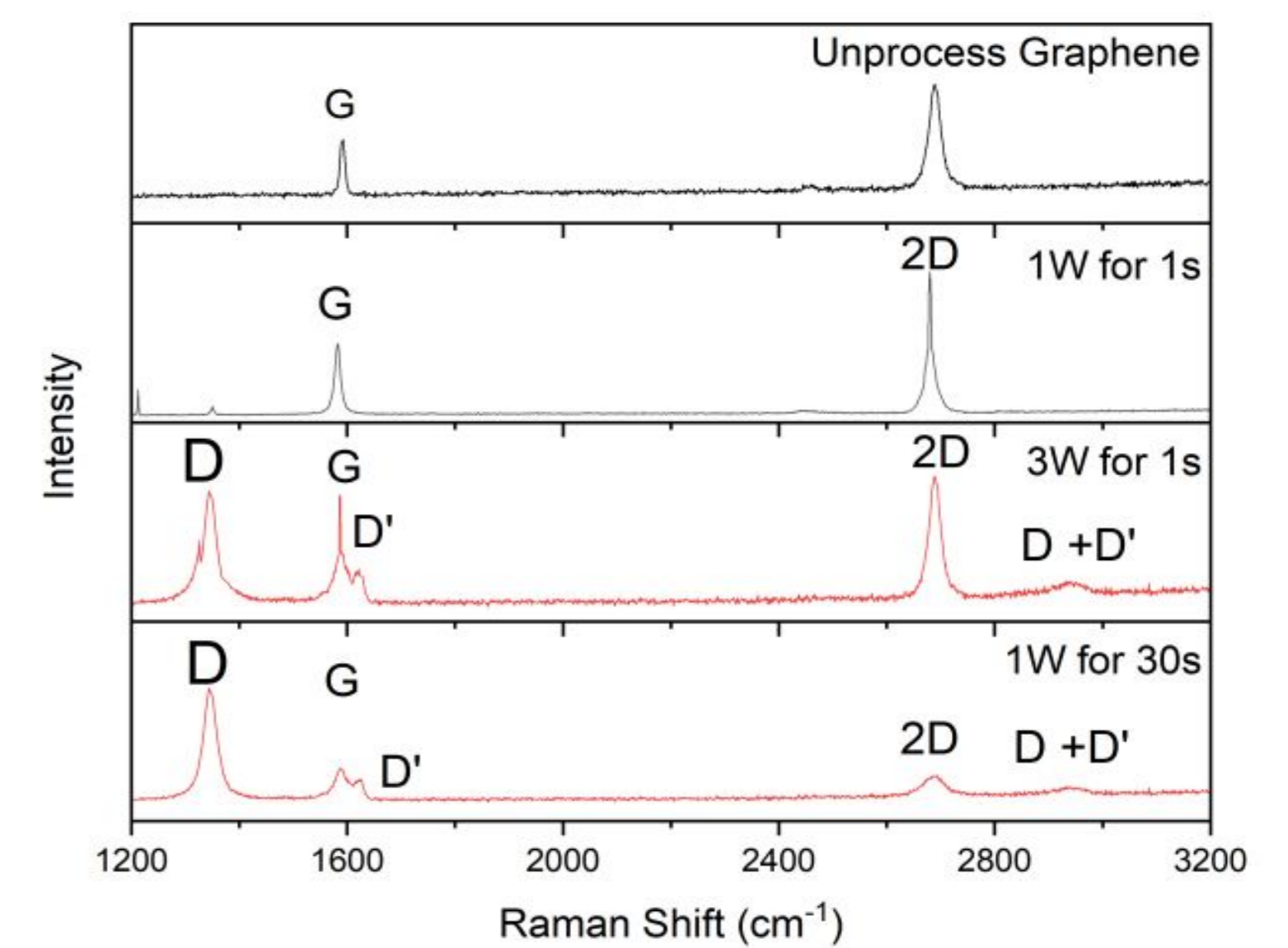


Fig.2: Raman Spectra of graphene prior to processing and after reactive ion etching at various powers and times

Sample	Interdefect Distance (nm)	I_D/I_G
0.5W/1s	35.6	0.04
1W/1s	26.2	0.2
2W/1s	18.4	0.8
3W/1s	10.6	1.3
1W/30s	6.2	4.5

Table 1: Defect Density and I_D/I_G ratios for etched samples

Atomic force microscopy and Scanning electron microscopy

AFM was performed on the most defected graphene samples and was unable to ascertain any information regarding the defects on the graphene surface. This was most likely due to the defects being beyond the resolution of the instrument or from issues due to chemical reactions on the surface. Similar was observed in the case of SEM where the resolution of the instrument used was not sufficient in order to determine the size and position of hole on the graphene surface. However, an interesting phenomena was observed where holes in the graphene sheet were produced as a result of the exposure to the electron beam.

Conclusion

It was demonstrated that even at low powers, reactive ion etching with Argon resulted in an increase in defects. Through increasing the power and etching time it was observed that the defect density could be increased. However, AFM and SEM were not able to provide any tangible results due to technical limitations.

With regards to further work, TEM or STEM is necessary in order to get the resolution down to a sufficient level so it is possible to measure and analyse pores that are around 1nm in size[3]. It should also be noted that graphene will only be able to provide limited benefit in this area with established techniques very widely used that are low in cost. It will therefore be necessary to integrate graphene with other in vitro BBB devices in order to produce a better representation of the barrier and all the transport mechanisms that are at work (see Fig.1).

Acknowledgments

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