Development of novel monophasic hybrid membranes for improved artificial kidney devices

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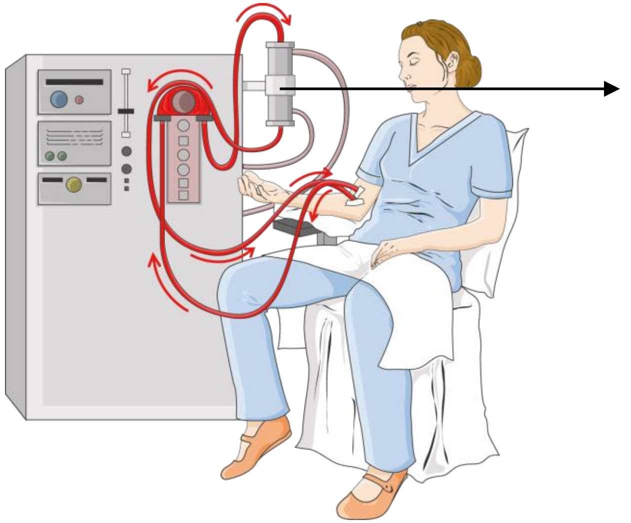
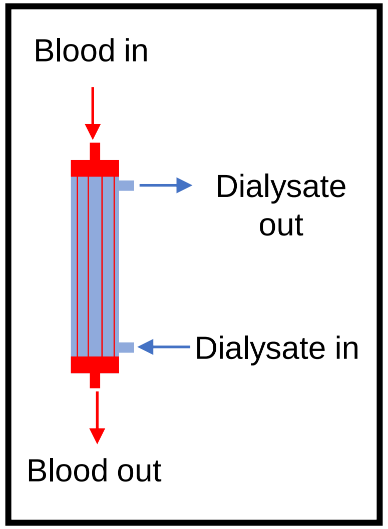
Hemodialysis (HD)

Most widely applied treatment for end stage renal disease (ESRD)

Hemodialysis machine (Kolff, 1945)

4 hours, 3 days/week





Uremic toxins (UT)

Classification	Solute	MW (Da)
Small molecules	Urea Creatinine Phosphate	< 500
Middle molecules	Vitamin B12 β2 macroglobulin	> 500
Protein-bound uremic toxins (PBUTs)	p-cresyl sulphate Indoxyl sulfate Hippuric acid	Most < 500

← Efficient in the removal of small uremic toxins

← Inefficient in the removal of many middle molecules

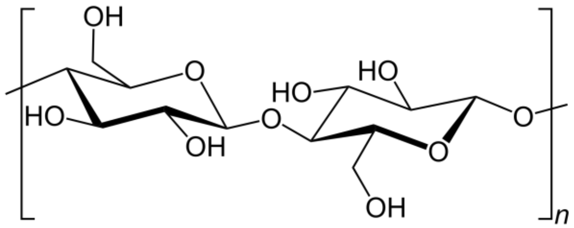
← Do not remove any PBUT

Two-fold goal:

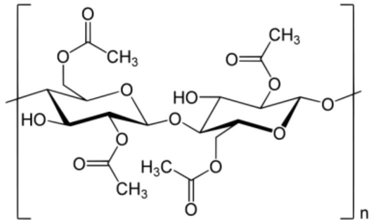
1. Selective mass transfer properties
2. Enhanced hemocompatibility

M. Faria & **M. N. Pinho** (2020) → DOI: 10.1016/j.trsl.2020.09.001

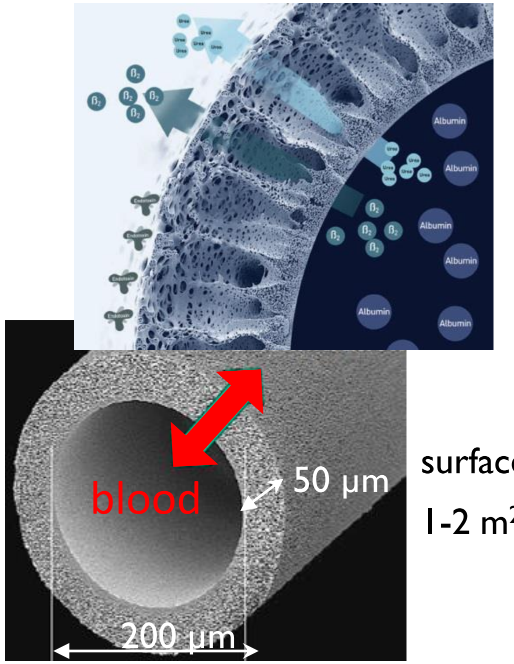
Cellulose



Cellulose acetate



Synthetic polymers



microporous polysulfone

surface area

1-2 m^2

F3® (Fresenius, Germany)

- polysulfone (PS)
- polyacrylonitrile (PAN)
- polyether-sulfone (PES)
- poly(methyl methacrylate) (PMMA)
- ethylenevinylalcohol (EVAL)
- polyesterpolymeralloy (PEPA)
- cellulose triacetate (CTA)

M. Faria, C. Moreira, T. Eusébio, P. Brogueira and **M. N. Pinho** (2020) → DOI: 10.1007/s10570-020-02985-2
M. Faria & **M. N. Pinho** (2020) → DOI: 10.1016/j.trsl.2020.09.001

AIM

Development of novel monophasic hybrid cellulose acetate silica ($CASiO_2$) membranes

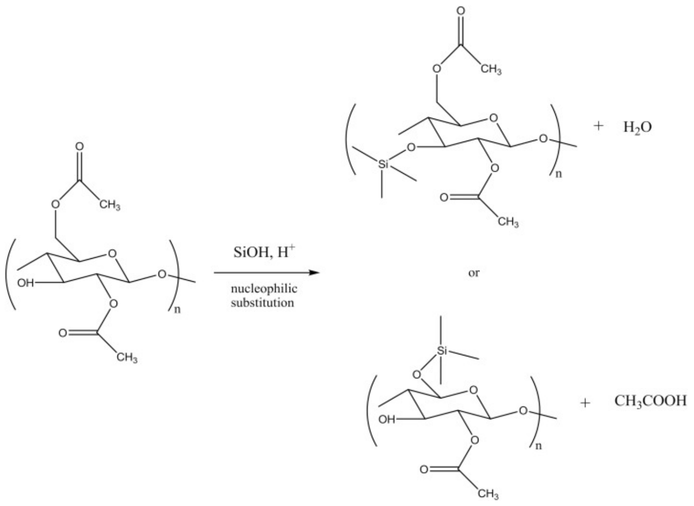
How to make hybrid asymmetric CA based membranes?

By coupling two methods:

- <u>Sol-gel technique</u> → covalently bond silica to cellulose acetate (hybrid membranes)
- <u>Wet phase inversion</u> → responsible for the membranes' asymmetric properties

$$\equiv Si - OH + OH^- \xrightarrow{fast} \equiv Si - O^- + H_2O$$

$$\equiv Si - O^- + HO - Si \xrightarrow{slow} \equiv Si - O - Si \equiv + OH^-$$



G. Mendes, **M. Faria**, A. Carvalho, M. C. Gonçalves & **M. N. Pinho** (2018) → DOI: 10.1016/j.carbpol.2018.02.030

METHODS

Membrane synthesis:

Preparation of monophasic hybrid cellulose acetate silica ($CASiO_2$) membranes by an innovative method which combines sol-gel and phase inversion techniques.

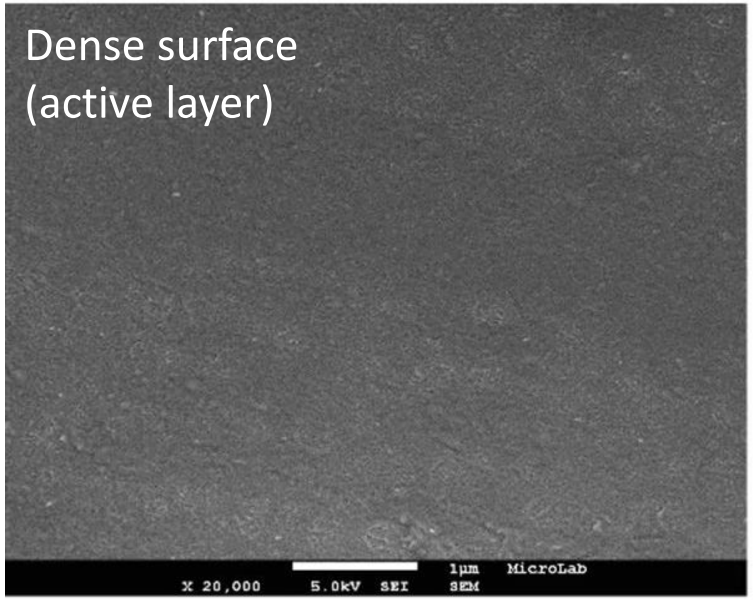
Casting solution:
- Cellulose acetate, formamide, acetone
- 0, 5, 11 and 18 wt% of Silica (SiO_2)

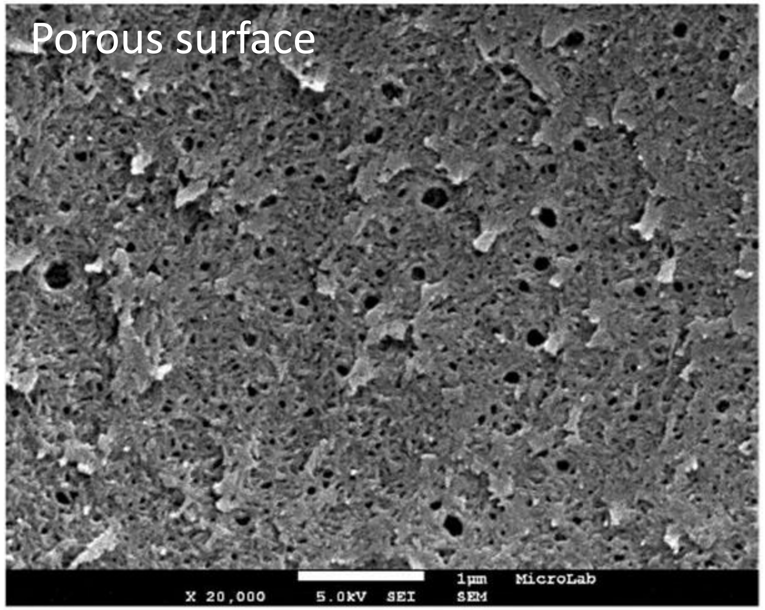
Casting conditions:
- Room temperature
- Solvent evaporation time 30s

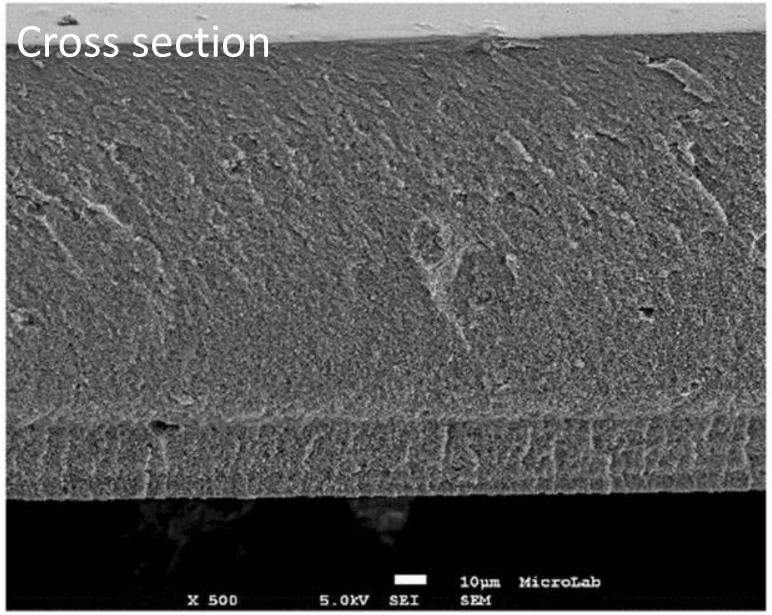
Membrane characterization:

- Hydraulic permeability (L_p)
- Rejection coefficients: urea and BSA
- Surface morphology: Scanning Electronic Microscopy (SEM)
- Hemocompatibility evaluation: Hemolysis index (HI), Thrombosis degree and Platelet interaction (ISO 10993-4:2002)

Surface morphology and cross section structure: SEM







An active dense layer, a porous layer and asymmetric cross sections were identified in all membranes similar to ones of CASiO$_2$-11

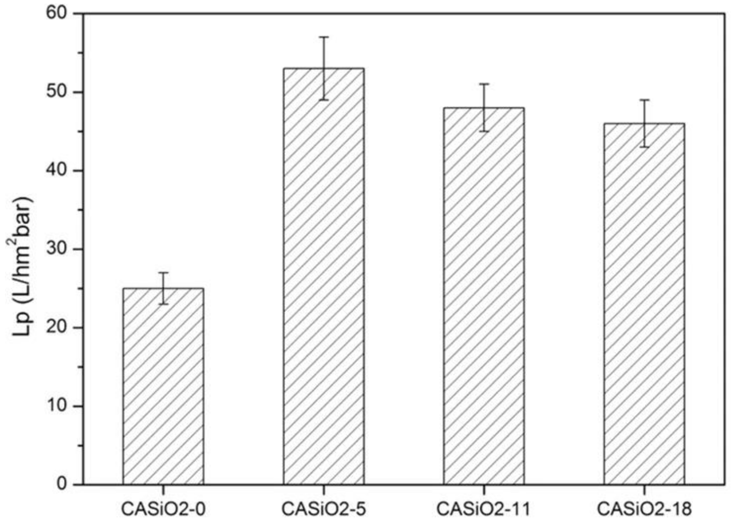
M. Faria, C. Moreira, T. Eusébio, P. Brogueira and **M. N. Pinho** (2020) → DOI: 10.1007/s10570-020-02985-2

Permeability experiments

Hydraulic permeability (L_p):

$$L_p = \frac{J_{pw}}{\Delta P}$$

obtained by the slope of the straight line of pure water permeate fluxes (J_{pw}) as a function of the transmembrane pressure (ΔP).



Addition of 5 wt% silica was enough to increase L_p of membranes

Rejection coefficients:

$$f = \frac{C_f - C_p}{C_f}$$

obtained by two parameters: C_f and C_p are the solute concentrations in the bulk of the feed solution and of the permeate solution, respectively.

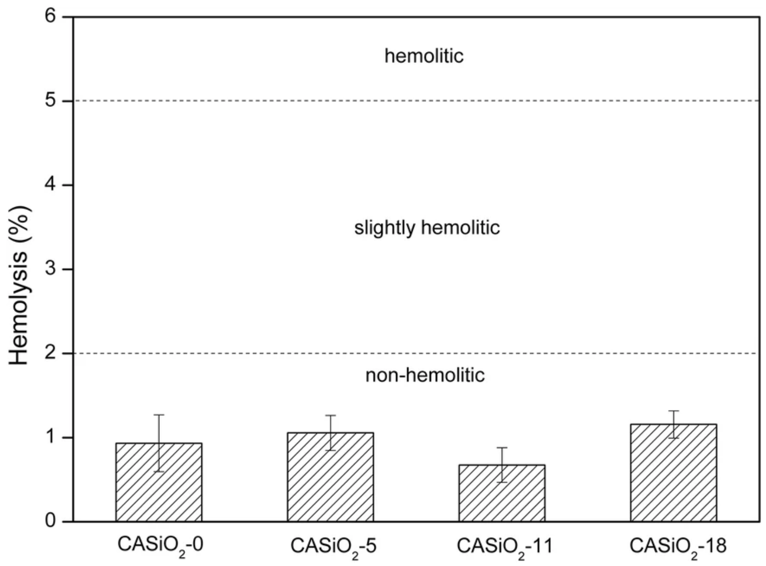
	membrane			
f (%)	$CASiO_2$-0	$CASiO_2$-5	$CASiO_2$-11	$CASiO_2$-18
urea	2.0 ± 0.4	0.2 ± 0.1	0.3 ± 0.1	0.3 ± 0.1
BSA	98 ± 2	99 ± 1	99 ± 1	99 ± 1

Urea was permeated by all membranes
BSA was rejected by all membranes

M. Faria, C. Moreira, T. Eusébio, P. Brogueira and **M. N. Pinho** (2020) → DOI: 10.1007/s10570-020-02985-2

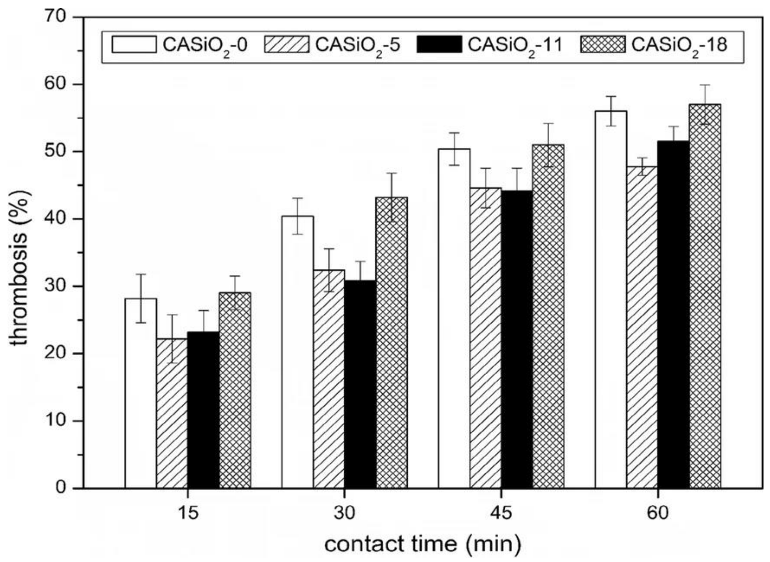
Hemocompatibility

Hemolysis index (HI):



All the membranes were non-hemolytic with (HI<2)

Thrombosis degree:

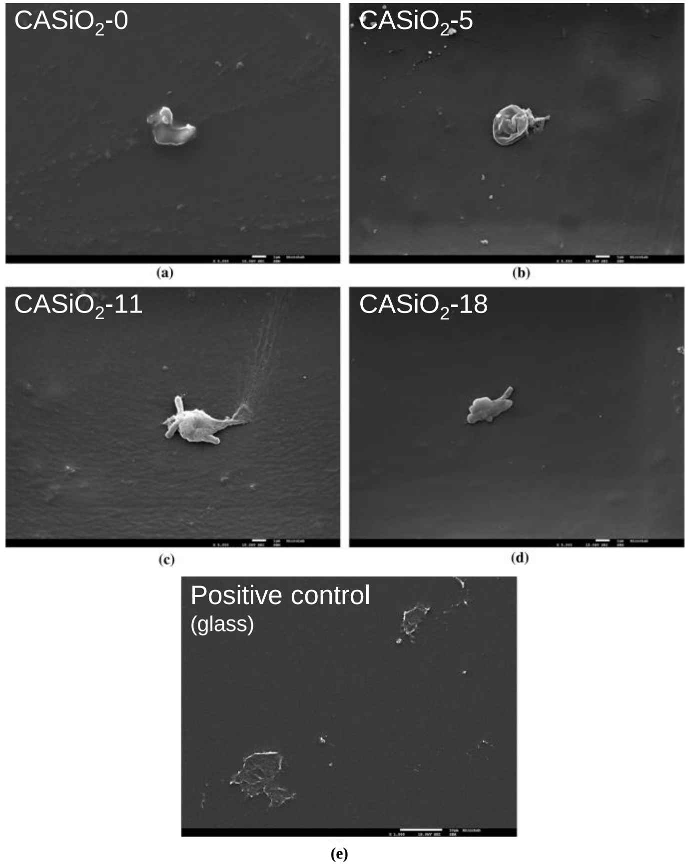


For blood contact time of 15 mins the thrombosis degree of all $CASiO_2$ membranes is lower than 30% of the positive control.

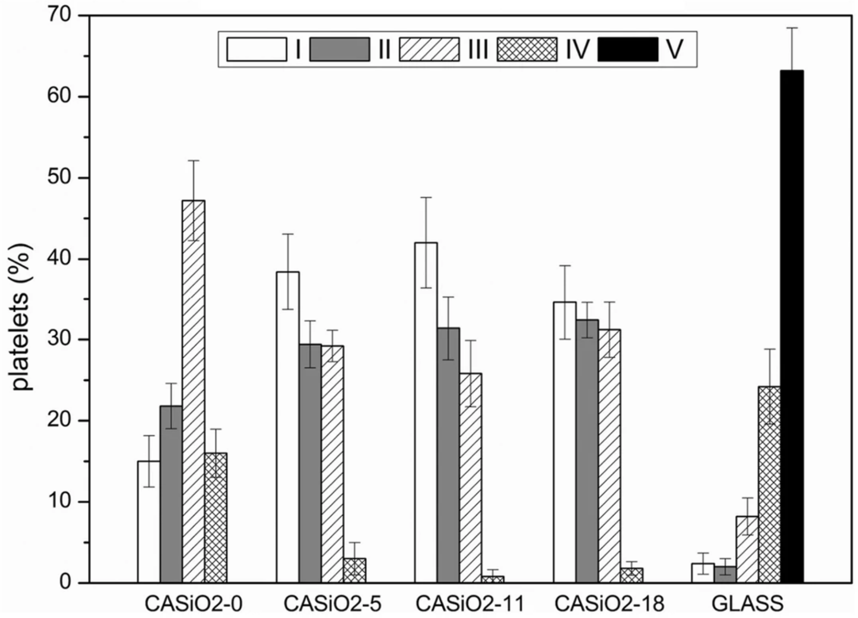
M. Faria, C. Moreira, T. Eusébio, P. Brogueira and **M. N. Pinho** (2020) → DOI: 10.1007/s10570-020-02985-2

Hemocompatibility

Platelet activation:



SEM images (×5000 magnification) of the $CASiO_2$ membranes' active layer surface after 30 min of contact



None of the membranes present platelets in the highest stage of activation (fully spread)

Number of platelets in the third stage is reduced by the introduction of silica

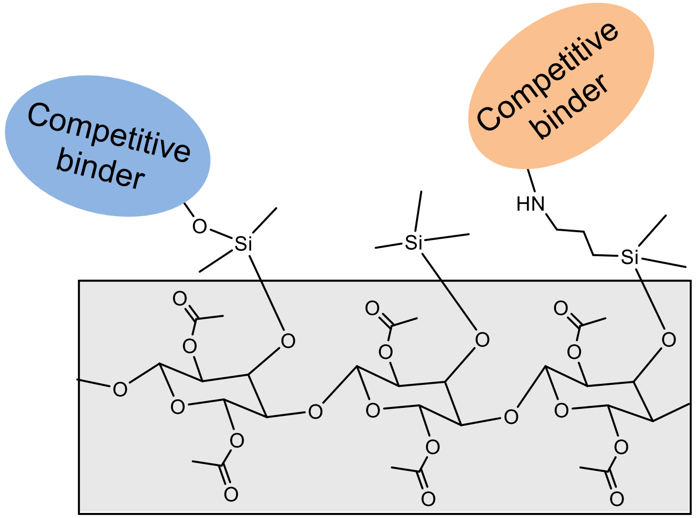
M. Faria, C. Moreira, T. Eusébio, P. Brogueira and **M. N. Pinho** (2020) → DOI: 10.1007/s10570-020-02985-2

MAIN CONCLUSION

- SEM confirmed asymmetric membrane cross-section structures.
- A thin active dense layer and a larger porous layer were identified in all membranes.
- Permeation studies show that the incorporation of SiO_2 into CA membranes increased the hydraulic permeability of the $CASiO_2$ membranes.
- Urea was fully permeated by all hybrid $CASiO_2$ membranes.
- BSA was totally rejected by all hybrid $CASiO_2$ membranes.
- Regarding the hemocompatibility, all $CASiO_2$ membranes were non-hemolytic, low thrombogenic and did not promote the highest stages of platelet activation.

ONGOING WORK

- Development of other novel monophasic hybrid cellulose acetate-based ($CA\text{-}SiO_2\text{-}(CH_2)_3NH_2$) membranes, using others precursors [e.g.: (APTES, 3-(aminopropyl)triethoxysilane].



- Development of Competitive binding membranes for enhanced removal Protein Bound Uremic Toxins.

M. Faria & **M. N. Pinho** (2020) → DOI: 10.1016/j.trsl.2020.09.001
M. C. Andrade, J. C. Pereira, N. Almeida, P. Marques, **M. Faria** and M. C. Gonçalves (2021) → 10.1016/j.carbpol.2021.117813

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Thank you!

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