OPTIMIZATION OF CELLULOSE ACETATE NANOFILTRATION MEMBRANES FOR MICROPOLLUTANT REMOVAL VIA GENETIC ALGORITHMS AND HIGH THROUGHPUT EXPERIMENTATION

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Abstract

Nanofiltration (NF) and reverse osmosis (RO) membranes have a high potential to remove low molecular weight trace contaminants in water that cannot be removed efficiently by conventional biological or physico-chemical treatments. However, membrane performance depends on several parameters involved in membrane synthesis. Multi-parameter optimization strategies, such as genetic algorithms (GAs) are extremely promising to minimize time and material consumption to direct membrane synthesis towards better separation properties (selectivity) of the targeted compounds combined with useful fluxes.

Cellulose acetate membranes were prepared via phase inversion. The optimized parameters included compositional (polymer concentration, solvent) and also, for first time when using GA as optimization strategy in membrane synthesis, non-compositional on the level of the

membrane synthesis process and post treatment (temperature, annealing time), which have a great impact on membrane performance.

Dead-end filtrations were carried out to evaluate membrane performance to retain ibuprofen in water by using High-Throughput experimentation (HT), which enables parallel testing and rapid acquisition of data sets and minimize time and material consumption. Ibuprofen was selected as it is one of the smallest molecules from relevant micropollutants present in drinking water. As result, membranes with ibuprofen retention up to 96% and permeabilities in the normal range of cellulose acetate (CA)-based reverse osmosis membranes were obtained, which also showed promising NaCl retention and twice the permeability compared to membranes prepared via a classical optimization parameter-by-parameter.

Keywords: nanofiltration, optimization, high throughput, micropollutants, water

1. Introduction

The currently and since years growing water demand worldwide, together with new and more strict regulations for potable and waste water levels, leads to the need of better cleaning technologies to decrease the concentration of micropollutants (pharmaceutical active compounds, endocrine disrupting compounds, etc) in water streams. These micropollutants are mostly of anthropogenic origin from industrial or domestic waste, including also their metabolites or sub-products, mostly in unknown concentrations. Their presence in water has an impact in environmental and human health. The prioritisation of organic micropollutants removal from surface and ground water is motivated by different criteria, such as their toxicity, concentration and the human perception of their presence in drinking water. [1]

Pressure-driven membrane-based technologies, as nanofiltration (NF) and reverse osmosis (RO), are well positioned to remove trace contaminants. Cellulose acetate (CA) is a common polymer used for NF and RO membranes. [2-3] Some are already commercially available since the 70s. [4] CA is cheap, presents relatively good resistance against chlorinated agents commonly used to disinfect water and is obtained from sustainable sources. However, there are some existing challenges, even still present nowadays, such as the need of an improved chemical stability and a high rejection of organic compounds combined with high water fluxes. Asymmetric membranes, consisting on a thin dense layer that determines the selectivity above a porous sublayer acting as support and providing mechanical stability, are interesting for these applications. [5] They are commonly prepared via phase inversion, which comprises the controlled transformation of a thermodynamically stable polymeric solution into a solid porous phase. [6] The final performance, directly linked to the structure, depends on multiple factors, including the composition of the polymeric solution (solvents, polymer concentration, additives) and non-compositional parameters at the level of the membrane synthesis process and post-treatment (evaporation time, temperature, annealing time). [7-8]

This multi-parameter optimization is complex as well as time and effort consuming. Combinatorial techniques and high throughput experimentation (HT) offer an interesting and efficient approach to direct the search. Combinatorial techniques and self-adaptive evolutionary strategies allow the search in a multi-dimensional solution space, focused in the regions that appear to be the most promising. Genetic Algorithms (GA) are stochastic search techniques inspired by the principles of evolution and natural selection found in nature. The successive generations of experiments are created by applying evolutionary operators (mutation and cross-over). A membrane that is experimentally found to be more successful will have more offspring and more variants in the following generation of experiments.

Populations thus evolve in a self-adaptive way towards the optimal solution. [9] Genetic algorithms have already been used in the pharmaceutical industry, [10] material development [11] and catalysis [10] leading to successful implementation. These tools have also proven to be extremely useful in membrane technology to develop better performing membranes, directing membrane composition towards improved separation properties. [13-15] In such an approach, it is possible to obtain maximum output while minimizing time and material consumption. [14] Also they have been used to select the operating variables of the process to optimize the performance of the membrane system. **[16]**

Despite their potential, the use of these optimization strategies would be extremely time and material consuming. The availability of HT experimentation enables rapid and accurate collection of large data sets, essential for the implementation of combinatorial synthesis, together with miniaturization (cost and waste reduction). [16-17]

The aim of this work is the optimization of CA-based NF/RO membranes prepared via phase inversion to be applied for salt and micropollutants removal in aqueous streams. The influence of both compositional and, for first time, non-compositional parameters will be explored by using GA. Membrane performance for ibuprofen retention from water as a test case will be determined. Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID). It is selected as it is one of the smallest molecules of relevant micropollutants currently present in drinking water. [18] Its successful removal may also indicate retention of all other micropollutants present in the water. Moreover, ibuprofen is the third most consumed pharmaceutical worldwide. [19] Although its concentration in water is normally below the 'Human Health Limit' (HHL), a general concern about their presence in drinking water exists due to the lack of detailed knowledge about the potential mixture toxicity, which occurs for

combinations of certain pharmaceutical compounds that lead to health risks despite being present in very low concentrations. [18] Finally, for selected cases, the membrane performance will be also evaluated for NaCl retention in water in order to compare it with the performance obtained via a classical optimization strategy.

2. Materials and methods

2.1. Reagents

C A (39.8 wt. % acetyl, average M_n ~30,000) was purchased from Sigma-Aldrich (Belgium). Acetone (Chem-Lab, Belgium) and 1,4-Dioxane (Riedel-de Haën, Germany) were used as solvents and methanol (Acros Organics, Belgium) as non-solvent. All were of analytical grade and used without further purification. 4-isobutyl-alpha-methylphenylacetic acid 99% (Ibuprofen) was acquired from Alfa Aesar (France) and sodium chloride 99 % (NaCl) from Sigma-Aldrich (Belgium).

2.2. Membrane synthesis and post-treatment

Membrane solutions consist of CA dissolved in a mixture of solvents/non-solvents in a variable ratio. The polymer content ranges from 12 to 25 wt% and the methanol content between 0 and 25 wt%. Acetone concentration was kept constant at 20 wt% as it is a common solvent for CA and had been fixed in CA membrane formulations in previous work. [20] Dioxane completes the composition up to 100 wt%.

CA membranes were prepared via phase inversion. A 250 µm thick film of the polymeric solution was deposited on top of a polypropylene/polyethylene non woven support (Viledon FO2471, Freudenberg, Germany) impregnated with methanol, by using a custom-build blade knife and an automatic film coater permitting the simultaneous casting of up to 8 membrane

solutions (Braive Instruments, Belgium) at a low casting speed (0.67 m/min). After a certain evaporation time (30, 60, 90 or 120 sec), the nascent films were immersed in a coagulation bath (distilled water at 4 °C) to induce the polymer precipitation and were kept there for 20 min. Afterwards a thermal annealing treatment followed, by immersing the membranes during a certain fixed time (2, 6, 10 or 14 minutes) in a water bath at constant temperature (65, 70, 75, 80 or 85 °C). The membranes were stored in distilled water at room temperature until use.

2.3. High-throughput filtration experiments

Membrane performance was evaluated in dead-end filtration experiments of feed solutions of 5 mg/l ibuprofen in water. They were carried out by using an in-house designed High-Throughput module (figure 1) built in collaboration with Agila (Belgium). It allows the simultaneous execution of 16 membrane filtrations and the minimization of membrane size (1,767 cm^2 membrane active area). To ensure a tight sealing, porous metallic plates were used as support for mounting membranes which were sealed with Viton O-rings. The feed solution was constantly stirred at 700 r. p. m to minimize concentration polarization and fouling.

The experiments were carried out at room temperature and at constant pressure (40 bars), provided by N_2. Permeates were collected as a function of time in closed glass vials, weighed and analyzed. The fraction collected during the first 15 minutes was discarded. All experiments were carried out in duplicate. In case that the variability of the measurements was higher than a 10% relative standard deviation (RSD) a third replicate was done. Permeabilities ($Lm^{-2}h^{-1}bar^{-1}$) were determined gravimetrically. Retentions were calculated as (1-Cp/Cf)*100% where Cf and Cp refer to the solute concentration of the initial feed and of the permeate respectively. Additional filtration experiments were done with a 5g/l NaCl in water at 40 bars.

2.4. Equipment

Ibuprofen concentration was determined on a Fluorolog -3-Model FL3-22 spectrofluorimeter (OPTILAN, The Netherlands) with a xenon lamp. [21] The intensity of the fluorescence emission at 290 nm was measured using quartz cells. The excitation wavelength was 224 nm. The slits were set at 12 nm. Spectra acquisition and data treatment were processed with the FluorEssence^{TM} software version 2.1 (HoribaJobin Yvon, USA).

NaCl concentration was determined by using a Consort K620 conductimeter. It was first calibrated using a 0,01M KCL solution at 20°C. All the samples were also measured at 20°C. The measured values were automatically corrected to the standard temperature of 25°C.

2.4. Evaluation of membrane performance

Membrane performance was evaluated with an objective function (OF) that combines the permeability (P) and the retention (R). The threshold retention ($R_{threshold}$) was 50 % (A). The target performance (R_{target}) was defined as 100 % solute retention and a water permeability (P_{target}) of 2 $Lm^{-2}h^{-1}bar^{-1}$ (B) (figure 2a). In order to adjust the weight of each component in the OF, the measured values of permeability ($P_{measured}$) and retention ($R_{measured}$) of the membranes were transformed to new coordinates ranging from 0 to 100 (C_1, C_2) according to the following equations:

$$C_1 = \left(\frac{P_{measured}}{P_{target}}\right) x\ 100 \quad (1)$$

$$C_2 = \left(\frac{R_{measured} - R_{threshold}}{R_{target} - R_{threshold}}\right) \times 100 \quad (2)$$

If C2 had a negative sign (retention below the threshold) it was given a value of zero. [13]

The OF values were calculated by the subtraction of the distance BC from AB in the coordinate space , following the formula (equation 3):

$$OF = AB - BC = \sqrt{((B1 - A1)^2 + (B2 - A2)^2} - \sqrt{(B1 - C1)^2 + (B2 - C2)^2} \quad (3)$$

Where A, B and C coordinates after transformation by applying eq. 1 and 2 are (0, 0), (100, 100) and (C_1, C_2) respectively. The calculation of OF in this particular case is:

$$OF = AB - BC = \sqrt{100^2 + 100^2} - \sqrt{(100 - C1)^2 + (100 - C2)^2}$$

Therefore, the closer the measured and target values are, the higher will the OF value be (figure 2b).

2.5 Membrane optimization

The combinatorial optimization of the membranes was carried out by applying a GA, reducing the time and effort required in a complete systematic 'one-by-one' screening of each parameter. The first generation of 48 membranes was created by an algorithm in the same way as reported in previous work. [14] An overview of the GA optimization steps is presented in figure 3.

The algorithm code was created using an excel spreadsheet. Each membrane is specified by an array of 5 values, including 2 compositional parameters (CA and methanol concentration, respectively polymer and non-solvent) and 3 non-compositional ones (evaporation time prior to coagulation, annealing time and annealing temperature). The design space is only 5 dimensional, as one of the compositional parameters is dependent due to the constraint to

have a composition total of 100 wt%: the dioxane concentration is obtained by subtracting the concentrations of CA, methanol, and acetone (constant at 20 wt %) from 100. The non-compositional parameters were considered as discrete variables due to technical aspects, since the selection from a continuous range of values would be not practically feasible in an efficient manner with reasonable throughput. From an operational point of view, it would also be extremely difficult to differentiate accurately between two annealing times differing in a few seconds only without significant experimental error or two annealing temperatures differing in one degree only.

The parents for every next generation were selected with the roulette wheel method, proportional to their fitness (OF). In the present study, only crossover and quantitative mutation were applied. Qualitative mutation was not considered as it involves the addition or elimination of one of the components. In our setting, the exclusion of one of the parameters would lead to an unfeasible combination (for instance, lacking annealing time or polymer). Crossover creates new individuals by exchanging a fragment of the digits between two individuals at a random position in the sequence of parameters. In quantitative mutation (hereafter referred to as mutation) the value for one randomly selected parameter changes. If the parameter is continuous, equation 4 is applied:

$$x_i^{new} = (1 + t) \cdot x_i^{old} \quad (4)$$

where t is a random number that controls both the direction and relative size of the mutation, sampled uniformly from the range [-0.5,+0.5].

The mutation method was inspired by the work of Wolf and co-workers. [25] However, in the present study, in order to improve coverage of the design space, values cannot just mutate by ±50%, but also by any smaller fraction. The compositional parameters were rounded to the nearest integer weight percentage, to avoid unfeasibly small variations of the compositional ratios, potentially exceeding the precision of the experimental method and apparatus. Whenever x_i^{new} is out of range, a new t is drawn and the procedure is repeated.

The mutation of a non-compositional, discrete parameter is calculated with equation 5. The value changes into the nearest higher or lower value, depending on the direction, determined by a random integer "s" which can be 1 or -1.

$$x_i^{new} = x_i^{old} + s(\Delta x_i^{old}) \quad (5)$$

In order to keep the value in the range, when the result of the quantitative mutation exceeds the lower or upper limits of the range, the algorithm automatically assigns the opposite extreme value.

The frequency to apply each operator (W_i) depends on the relationship between the values of OF_{best} and OF_{mean}, as expressed in equations 6-7:

$$W_{crossover} = \frac{B \times OF_{mean}}{OF_{best}} \quad (6)$$

$$W_{mutation} = 1 - W_{crossover} \quad (7)$$

B is a control parameter and is set to 1.

3. Results and discussion

The components of the membrane precursor solutions were selected based on literature results. Methanol was selected as non-solvent as the membranes produced with methanol exhibited higher permeabilities and on average relatively higher retentions (for NaCl) compared to membranes prepared with other non-solvents. [20] It is also known that incorporating additives to the casting solution permits obtaining CA membranes with a wide variety of molecular weight cut offs (MWCO) ranging from RO to UF. [22]

First generation

The 48 first generation membranes were generated stochastically. The population size was selected to be a multiple of 16 due to practical reasons, as the HT set ups permit 8 and 16 simultaneous membrane synthesis and testing simultaneously. In previous similar optimizations a population size of 64 was selected for 8 parameters. [15] Since the total number of parameters to be optimized is 6, 48 seems to be an adequate population size. For each parameter, a value was randomly selected in the ranges presented in section 2.2. As result, a vector with 5 elements was obtained in each case, which corresponds to PI concentration, methanol concentration, evaporation time, annealing time and annealing temperature respectively. Note that although the independent parameters were each drawn from a uniform distribution, the resulting distribution of the dependent parameter dioxane is not uniform.

Some of the membranes in the first generation were defective, with extremely high permeabilities and practically no retentions. If the retention was lower than the threshold (50 %) the value 0 was assigned to the retention coordinate. However, since the permeability coordinate was always different than 0 (no threshold has been defined) it was still possible to calculate a value for the OF, in an attempt to not exclude very permeable membranes. If the permeability was higher than the target (2 $Lm^{-2}h^{-1}bar^{-1}$) and the retention was below the threshold, the permeability coordinate was set to '100' and the OF value for these cases was constant to avoid giving too much importance to the permeability. The best value (OF_{best}) was 86.2 obtained for membrane M1-8, with 87.73 % ibuprofen retention and 1.01 $Lm^{-2}h^{-1}bar^{-1}$ water permeability. The mean OF value (OF_{mean}) of this generation was 34.9, which is an indication of a relatively low overall performance. In view of the results, the membranes with the highest permeabilities generally have a relatively low polymer contents (12-15 wt %), which is in agreement with the literature. [23, 24] Nevertheless, membranes with a low polymer concentration do not always have a high permeability, as there are many other factors involved, which is exactly the reason of doing a combinatorial optimisation.

Second generation

The second generation was created by the application of evolutionary operators to the parent compositions (first generation). The $W_{crossover}$ and $W_{mutation}$ calculated with the OF_{best} and OF_{mean} values of the first generation were 0.59 and 0.41 respectively. All the 48 new combinations of the second generation led to thermodynamically stable solutions. Therefore, the 48 membranes could be synthesized although two of them presented defects, leading to a zero OF value. The OF_{best} value in the second generation was 63.4, clearly lower than in the first one. The same effect has been observed in previous work. [14] The OF_{mean} was 31.8,

slightly lower than the first generation value (34.9), which indicates that in the second generation the overall performance of the population has not yet improved. The membrane with the best OF, however, has a very good retention (90.3 %) and a not very low permeability (0.49 $Lm^{-2}h^{-1}bar^{-1}$). The reason of this membrane having a low OF (63.4) value is that the permeability target (2 $Lm^{-2}h^{-1}bar^{-1}$) is very ambitious for CA membranes prepared in these conditions according to literature. [8, 20]

Third generation

The next 48 membranes of the third generation were synthesized and tested. Based on the results of the second generation, $W_{crossover}$ and $W_{mutation}$ were both 0.5. All of the 48 membranes could be cast but 6 showed defects and lack of stability. The OF_{best} and OF_{mean} were 89.5 and 37.7 respectively, which are the highest values of the three generations. These results indicate an improvement of the overall membrane performance. The best performing membrane has a retention of 82.5 % and a high water permeability (1.23 $Lm^{-2}h^{-1}bar^{-1}$).

Fourth generation

From the results of the third generation, $W_{crossover}$ and $W_{mutation}$ were calculated (0.37 and 0.63 respectively). A number of 18 membranes were obtained by applying mutation and 30 by applying crossover. The probability of applying the crossover operator, which creates more diversity in the population, was lower than in the previous generations. All 48 membranes could be tested and none presented defects. The OF_{mean}/OF_{best} ratio (OF_{mean} is 43.2 and OF_{best} 85.32) is higher compared to the first and third generation (0.506, 0.405 and 0.366 respectively). Also, according to a Student t-test, the OF values in the fourth generation are higher than random sampling (first generation) at a 5% significance level. The retention of the

membrane with the best performance is 77.8 and its permeability 1.31 $Lm^{-2}h^{-1}bar^{-1}$. Nevertheless, most of the membranes in this generation present, in general, higher retentions than in the preceding ones with only 8 membranes below the retention threshold, compared to 10, 15 and 17 in the first, second and third generations respectively. However, the permeabilities are in general, lower.

The summary of the results of the 4 generations is presented in table 1

Comparison of the four generations and global results

The comparison of all generations indicates that the most promising results have been obtained in the 4th generation (highest OF_{mean}, and also very high OF_{best}, with the membranes with the higher average retentions and equal average trend in permeability). Also, in view of the results presented in figure 4, the general trend in the first two generations is to obtain membranes with higher permeabilities. In particular in the third generation, the retentions seem to be on average higher than in the second. In the same figure, it is possible to observe that the membrane with the highest retention (98.3 %), was achieved in the fourth generation, although with a low permeability (0.09 $Lm^{-2}h^{-1}bar^{-1}$).

The distribution of the membrane performance over the 4 generations is presented in figure 5. It shows clearly that there is a general increase in the OF values in the 4th generation, as more membranes have an OF higher than 50, as compared to the other generations. The highest OF value corresponds to a membrane of the 3rd generation. Compared to earlier work carried out at our laboratories, the progress towards better performing membranes seems to be not as fast as for our other studies in which such membranes were directly excluded to create the next generation. [14] They were not discarded *a priori* in this work as they might probably lead to

certain combinations for promising offspring membranes. Besides the introduction of the non-compositional parameters as variables, the fact of still consider membranes with relatively high permeability and retentions lower than the threshold could be a reason to slow down the evolution.

The membranes with the top 10 OF values of the 192 membranes (4 generations) are presented in table 2. In general, the membranes with the highest OFs present ibuprofen retentions below 90 %. However, the 7th membrane in the ranking OF (M2-12), has a very good retention (90 %) combined with a reasonable permeability (0.49 $Lm^{-2}h^{-1}bar^{-1}$), being comparable to the values for CA-based membranes for reverse osmosis applications. [20] It is important to note that the permeability target in this optimization was too ambitious; therefore high permeabilities were only obtained at the expense of retention.

Within the group of 10 membranes with the highest permeabilities (table 3), a low polymer concentration (maximum 15 wt %) seems to be a common feature (9 of 10 membranes). It is known that an increase in polymer concentration in the membranes solutions leads to denser membranes, thus with lower permeabilities. [7] The methanol content (non-solvent) varies, since both very low concentration (3 wt %) and high concentrations (≥20 wt %) are found in the list. Most of the membranes present relatively low evaporation times (7 of 10 membranes have evaporation times up to 60 seconds). The minimum evaporation time (30 s) is overrepresented meanwhile the maximum evaporation time (120 s) is absent, which is in agreement with obtaining less dense (more permeable) membranes. Regarding the annealing treatment, in most of the cases it is a combination of relatively short times (mostly 2 or 6 minutes) and average temperatures (70-80). In this selection of membranes, a longer annealing time is only applied when the annealing temperature was low (65 °C).

The 10 membranes with the highest ibuprofen retentions are presented in table 4. In these cases, the polymer concentrations correspond to the upper range (between 18-22 wt %), with exception of the first membrane. In this particular case, the evaporation time is relatively long, which leads to a further evaporation of the volatile solvent and causes an increase in the polymer concentration near the membrane surface and a densification of the final structure of the top layer, which normally determines the selectivity. [7] All membranes except two have evaporation times of 60 seconds or higher. As for the membranes with the highest permeabilities, the effect of the methanol concentration is not straightforward. The thermal annealing, which has an essential influence in the selectivity of the membranes, is mostly carried out at average or high temperatures and, in half of the cases, at the longest times (14 minutes).

Application to water desalination

Since no publication on development of cellulose acetate-based membranes applied to ibuprofen separation has been found, NaCl filtration experiments were carried out in order to compare the performance of the obtained membranes with CA membranes in the literature optimized via classical methods to evaluate whether the membranes optimized by using GA lead to similar or improved performances.

A total of 5 membranes (the best membrane in terms of OF, and the two best ones for retention and permeability only of the total 192 candidates) were selected to perform NaCl filtration experiments in order to compare with earlier CA-membrane optimizations reported in the literature. The results are presented in table 5.

Membrane M3-47 retains 83% NaCl, which is as high as was obtained by Duarte and co-workers, while its water permeability is twice as high (1.2 relative to 0.6 $Lm^{-2}h^{-1}bar^{-1}$). Duarte et al. prepared 45 different membranes and performed a classical optimization by fixing all except one parameter and screened parameters one by one. None of those membranes reached performances (permeability combined with selectivity) as good as some of the best membranes in this work. This indicates that there are certain parameter combinations that can lead to membranes with better performances which were missed because of the traditional optimization approach, in which a narrower space of combinations was screened. The obtained results in this work demonstrate the potential of combinatorial techniques and self-adaptive evolutionary approaches as more powerful optimization tools, allowing a better exploration of a multidimensional exploring wider a higher dimensional space.

4. Conclusions

Combinatorial techniques and evolutionary search strategies together with the use of HT experimentation proved again to permit the efficient search of a multi-parameter space. Thanks to the availability of the HT set-ups the experimental work of this optimization is feasible in 3 months. In the present work, for the first time, also non-compositional parameters of the membrane synthesis process have been included in the GA- based optimization procedure. For most promising membranes (high permeability and/or high retention), the relationship between the values of compositional and non-compositional parameters and the trend in membrane performance is in agreement with the conclusions earlier reported in the literature. Over the four generations, an improvement of the overall performance of the results was observed, indicating a progress to find more promising combinations for the desired objective. This directed search has led to high-performance

membranes with retentions close to the target values. Also high permeabilities were obtained but not always combined with high retentions. It thus seems that the permeability target of 2 $Lm^{-2}h^{-1}bar^{-1}$ was too ambitious to be combined with a significant retention of the very small ibuprofen molecule.

Promising membranes were thus developed for the retention of micropollutants from aqueous streams with a good retention (up to 96%) of the small target compound ibuprofen, combined with a permeability of 0.7 $Lm^{-2}h^{-1}bar^{-1}$, which is in the normal range of CA-based reverse osmosis membranes. Moreover, a membrane was prepared with the same NaCl retention and, compared to a classical parameter-by-parameter optimization, twice the permeability value reported in the literature.

Further work on optimization of CA-membranes for these applications with other multi-parameter optimization strategies and machine learning methods) is currently on going in order to. evaluate which one leads to faster convergence and better results.

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