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Mathematical description of hydrogels' behavior for biomedical applications

Master's Thesis in Chemical Engineering

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Contents

List of Figures	v
List of Tables	ix
Sommario	xi
Abstract	xiii
Part I Ionotropic Gelation	1
1 Theory	3
1.1 Materials background	3
1.1.1 Alginate	3
1.1.2 Ruthenium Red	4
1.2 Ionotropic gelation	5
1.2.1 Capillary formation in ionotropic gels	6
1.2.2 Capillary formation: a mathematical model	9
2 Materials and Methods	15
2.1 Materials	15
2.2 Preparation of agarose gels	15
2.3 Preparation of alginate gels	16
2.3.1 “Random” gels	16
2.3.2 “Porous” gels	16
2.3.3 R value	17
2.4 Image analysis	17
2.4.1 Samples preparation	17
2.4.2 Analysis	18
2.5 Macroscopic Flow	18
3 Modeling	21
3.1 Pores formation	21

3.2	Macroscopic Flow	23
3.2.1	Darcy model	23
3.2.2	COMSOL model	24
3.2.3	Hagen-Poiseuille	24
3.2.4	COMSOL and Hagen-Poiseuille results comparison	26
4	Results and Discussion	27
4.1	Alginate Gels characterization	27
4.1.1	General porosity characterization	27
4.1.2	Evaluation of the pores diameter and density along the gel height	30
4.1.3	Qualitative observation on the copper gels	31
4.1.4	Modeling result	32
4.2	Macroscopic flow: experimental and modeling results	36
4.2.1	Experimental results	36
4.2.2	Modeling results	39
5	Conclusions	43
5.1	Ionotropic gelation conclusions	43
Part II Bioadhesion		45
6	Theory	47
6.1	Materials background	47
6.1.1	Carbopol 974-P NF	47
6.1.2	Agarose	48
6.2	Bioadhesion	49
6.2.1	Swelling	50
7	Materials and Methods	53
7.1	Materials	53
7.2	Tablets preparation	53
7.2.1	Preparation of "modified" test tablets	53
7.3	Preparation of agarose gels	55
7.4	Adhesion experiments	55
8	Modeling	59
8.1	Tablet hydration and swelling	59
8.1.1	Geometry	59
8.1.2	Equations	59
8.1.3	Initial conditions and boundaries	62

8.1.4	Diffusion coefficients	63
8.2	Elastic model	64
8.3	Models coupling	66
9	Results and Discussion	67
9.1	Bioadhesion: experimental studies	67
9.1.1	Experimental conditions reproduction	67
9.1.2	Modified Carbopol tablets	68
9.2	Modeling results	71
9.2.1	Tablet hydration, swelling and elastic response for the pure system	71
9.2.2	Tablet hydration, swelling and elastic response for the modified system	77
10	Conclusions	83
10.1	Bioadhesion conclusions	83
Part III	Final Remarks	85
11	Bioadhesion studies with ionotropic gels	87
12	General conclusions	91
13	Perspectives	95
Appendix A	Comsol model implementation	97
A.1	Aim	97
A.2	Model implementation	97
A.2.1	Physics and geometry	97
A.2.2	Global and local variables definition	100
A.2.3	Setting up the Transport of Concentrate Species	101
A.2.4	Setting up the Deformed Geometry	103
A.2.5	Mesh	104
A.2.6	Study	106
Bibliography		107

List of Figures

1.1	Alginates structures.	4
1.2	Ammoniated ruthenium oxychloride molecule, also known as Ruthenium Red.	4
1.3	“Egg-box” model [5].	5
1.4	Qualitative structure difference in an M-rich alginate (left) and G-rich alginate (right) [6].	5
1.5	How to form alginate porous gel.	7
1.6	Pores initiation on the top and development along the gel height. Adapted from [7].	7
1.7	Convective torus pattern generated close to the gelling surface (left). Schematical representation of torus cells and capillary structure: spatially organized tori form a hexagonal flow pattern which moves downwards with the front of freshly formed gel (right) [9].	8
1.8	Miscibility gap with nucleation and growth separation mechanism (zone 2) and spinodal region (zone 1).	9
1.9	Coordinate system of the hydrodynamic model [16].	10
2.1	Alginate porous gel non-treated (left) and treated (right) with Ruthenium Red.	18
2.2	Macroscopic flow homebuilt apparatus. Exploded view with a calcium gel (left); the assembled device with a copper gel (right).	19
3.1	Pore depth for a Calcium alginate gel.	22
3.2	Boundary conditions.	25
4.1	“R-diameter” (top), “R-pore density” (middle), “R-Holed Area” (bottom).	29

4.2	“Height-Diameter” (upper-left), “Height-Pore density” (upper-right), Height-Holed Area (bottom). The top, middle and bottom heights are approximately at 2, 10 and 17 mm respectively under the gel surface.	30
4.3	Macroscopic picture of the copper gel central behaviour, distinguishable for the lighter colour (left); microscopic picture at 180x (right).	31
4.4	Ionic solution concentration effect in the pores formation.	32
4.5	Alginate solution concentration effect in the pores formation.	33
4.6	Pore length Ca-gel (top-left), Cu-gel (top-right), Sr-gel (bottom) with ionic solutions concentration 0.1 M.	34
4.7	Minimum ionic solution concentration: Ca-gel (top-left), Cu-gel (top-right), Sr-gel (bottom).	35
4.8	Macroscopic flow: experimental results.	36
4.9	Alginate gel permeability as function of the pressure drop.	36
4.10	Macroscopic flow with HEC.	37
4.11	HEC solution flow curve at different concentrations.	38
4.12	Permeability with HEC.	39
4.13	Macroscopic flow: modeling with Darcy approach.	40
4.14	Macroscopic flow: modeling with Hagen-Poiseuille approach. Results comparison for Ca-gel(top), Cu-gel (middle) and Sr-gel (bottom).	41
6.1	Acrylic acid monomer unit (left) and neutralized Carbopol structure (right).	47
6.2	Effect of pH and Concentration on the Viscosity of Carbopol 974P NF Polymer Dispersion [23].	48
6.3	Agarose structure.	49
7.1	Tablet of freeze-dried Carbopol (left) and of non treated Carbopol (right).	55
7.2	Force vs time curve. The steel probe is first lowered onto the gel surface (a). Reached the a force of 0.05 N (b) the tablet is kept on the gel surface for a pre-definite time interval, 30 s in this case. (c) The probe is withdrawn until the tablet is detached from the gel (d) [17].	56
7.3	Force versus displacement time in a typical recorded behavior. The LEP (Linear Ending Point) is shown whereas “d” is the adhesion force (as in Figure 7.2) and “e” represent the complete detachment.	57
7.4	Alginate gel sliced (left) and fixed to the support (right).	58

7.5	Replacement of the ionic solution with HEC (left) and result (right).	58
8.1	Tablet hydration and swelling model, geometry. “ Ω_1 ” represent the tablet domain, “ Ω_2 ” the agarose domain. With “ $\partial\Omega$ ” are indicated the boundaries.	60
9.1	Contact time effect in the system Agarose-Carbopol.	67
9.2	Force (left) and weight gain (right) in the system Agarose-Modified Carbopol at contact time of 180 s.	68
9.3	Swelling tests for the Carbopol+NaCl tablets.	69
9.4	Comparison between experimental and modelled “weight gain”.	71
9.5	Mass fraction profiles in the agarose gel (top) and in the pure carbopol tablet (bottom).	72
9.6	Mass fraction of water (w_{1w}) and size enlargement at different contact times. a) Time 0 s, b) 10 s, c) 30 s, d) 60 s, e) 180 s, f) 300 s.	73
9.7	Force vs. displacement time. Experimental data and elastic model result at 10 s, 60 s and 180 s.	74
9.8	Generalized expression of E_0 function of the contact time.	75
9.9	Comparison between experimental and modeling results at contact time of 30 s: force prediction at the LEP (Linear Ending Point) condition.	76
9.10	Force and displacement time at the LEP condition at different contact time.	76
9.11	Generalized expression of α function of the Carbopol/NaCl concentration.	77
9.12	Experimental and modeling WG for the Carbopol/NaCl cases.	78
9.13	Generalized E_0 in the range [1:1, 1:100].	79
9.14	Comparison between experimental and modeling results, concentration 1:7 (first three) and 1:50 (last three).	80
9.15	Force and displacement time at the LEP condition at different Carbopol/NaCl concentrations.	81
11.1	Force - $\%Area_{holes}/Area_{tot}$ (left) and WG - $\%Area_{holes}/Area_{tot}$ (right).	87
11.2	Adhesion force (left) and weight gain (right) for alginate gels at R=2. Unmodified gel (blue triangle), washed with Milli-Q water (red square) and with HEC (black circle).	88
A.1	Space Dimension.	97
A.2	Physics choice.	98

A.3	Study Time.	98
A.4	Geometry creation.	99
A.5	Geometry.	99
A.6	Physics-geometry coupling.	100
A.7	Global definitions.	101
A.8	Transport of Concentrate Species in the domain 1.	101
A.9	Transport of Concentrate Species in the domain Ω_1 , definitions.	102
A.10	Stiff-spring boundary condition on domain 1.	103
A.11	Stiff-spring boundary condition on domain Ω_2	103
A.12	General Projection configuration.	104
A.13	Generated mesh with a Fillet of $100 \mu\text{m}$	105
A.14	Comparison between mesh deformation at 180 s with the standard geometry (left) and “Fillet” geometry (right).	105

List of Tables

3.1	Treml's parameters.	21
3.2	Kohler's model parameter for this work conditions	23
4.1	Gels analysed.	27
4.2	Porosity results from image analysis.	28
4.3	HEC viscosity in the test condition.	38
7.1	Mass relation NaCl:Carbopol for a tablet (350 mg).	54
9.1	Best fit diffusion coefficients.	71
9.2	Penetration length l_0 (at 10% of the interface concentration) and r_0 (average).	72
9.3	Calculated α values from Equation 9.2.	78

Sommario

Negli ultimi anni l'interesse verso gel macroporosi è cresciuto e ad oggi questi materiali vengono utilizzati in diverse applicazioni come, ad esempio, nel rilascio di farmaci, nella medicazione di ferite e nell'ingegneria dei tessuti. Una frazione significativa di queste sostanze è costituita da alginati, polisaccaridi estratti da alghe che, in presenza di ioni bivalenti, sono in grado di reticolare e formare "gel ionotropici". In certe condizioni di gelazione è possibile far sviluppare dei capillari dritti, di dimensioni macroscopiche, lungo tutta l'altezza del gel. L'utilizzo in ambito biomedico di questi particolari materiali fa sì che la loro produzione, e quindi il meccanismo di formazione, debba essere compreso a fondo per poterne modulare le caratteristiche e renderle idonee alle varie applicazioni.

Con lo scopo quindi di far luce su questo fenomeno, la morfologia di gel ionotropici di alginato, prodotti con ioni di tipo Ca^{2+} , Cu^{2+} , Sr^{2+} , è stata analizzata mediante analisi dell'immagine. I risultati ottenuti mostrano un'evoluzione delle caratteristiche di porosità in termini di diametro e densità dei pori e in termini di percentuale di area dei pori al variare dell'altezza del gel.

Visti inoltre i recenti utilizzi di gel ionotropici macroporosi a scopi di vascularizzazione e rimozione di essudato, in questo lavoro, i gel sono stati anche caratterizzati in termini di permeabilità. Allo scopo è stato messo a punto un metodo basato sulla semplice misura della quantità di fluido che attraversa il gel nell'unità di tempo. I risultati, anche in questo caso, evidenziano caratteristiche differenti a seconda dello ione utilizzato. Il flusso di fluido attraverso questi gel è stato inoltre modellato e comparato ai dati sperimentali.

Infine le diverse teorie proposte in letteratura per la descrizione della formazione dei capillari sono state analizzate e, in particolare una, la "teoria idrodinamica" è stata implementata in un modello. Questo è stato validato su dati sperimentali mostrando delle buone caratteristiche predittive e soprattutto mettendo in risalto le variabili che dominano il processo.

Un'altra importante proprietà impiegata in campo biomedico, che coinvolge idrogeli, è la bioadesione. Questo fenomeno avviene tra una parete biologica e una sostanza adesiva che, solitamente, è un materiale capace di rapida gelazione. Sebbene esistano in commercio farmaci che sfruttano questo meccanismo per rilasciare in modo controllato il principio attivo, non sono stati chiariti i fenomeni chimico fisici alla base del processo di adesione e quali siano i parametri che maggiormente lo influenzano.

In questo lavoro l'attenzione è stata focalizzata sull'importanza del trasporto di acqua dalla parete biologica, simulata da un idrogel, al materiale bioadesivo.

Diverse prove sperimentali sono state effettuate cercando di modulare la pressione osmotica del gel/adesivo risultante e aumentarne le caratteristiche di *swelling*.

È stato inoltre studiato l'effetto del cambiamento di trasporto dell'acqua, grazie al cambiamento di morfologia del gel simulante la parete biologica, sulle proprietà bioadesive.

Infine è stato sviluppato un modello simulante il trasporto dell'acqua, dello *swelling* e della prima risposta adesiva, di natura elastica, trovando un buon accordo con i dati sperimentali.

Abstract

Over the last years the interest in macroporous gel has been grown and nowadays these materials are used in various applications such as, for example, drug delivery, wounds dressing and tissue engineering. A significant fraction of these substances is constituted by alginates, polysaccharides extracted from algae that, in presence of divalent ions, are able to crosslink and form “ionotropic gels”. In certain gelation conditions it is possible to develop straight capillaries, of macroscopic dimensions, along the gel height. Considering that these particular materials are used in biomedical field, their production, and thus the formation mechanism, should be fully understood to be able to modulate their characteristics and to make them suitable for various applications. Therefore with the aim of making light on this phenomenon, the morphology of ionotropic gels of alginate, produced with ions Ca^{2+} , Cu^{2+} , Sr^{2+} , was analyzed with image analysis. The results obtained show an evolution of porosity, in terms of diameter, density of pores and in terms of percentage of holed area, along the gel height. Moreover seeing that in the last years these gels have been used for vascularization and exudate removing purposes, the gels were also characterized in terms of permeability. In order to do that, a method has been conceived and developed based on the simple measurement of the quantities of a fluid passing through the gel in the unit time. The results, even in this case, show different characteristics depending on the used ions. Furthermore the flow through these gels has also been modelled and compared to experimental data. Finally, the different theories describing the capillaries formation has been analysed and, in particular one, the “hydrodynamic theory” has been implemented in a model. This has been validated on experimental data, showing good predictive characteristics and, above all, highlighting the variables that dominate the process.

Another important property, which involves hydrogels in biomedical field, is bioadhesion. This phenomenon takes place between a wall and a biological adhesive substance which, usually, is a material capable of rapid gelation. Although there are several drugs on the market that use this mechanism to release the active substance in a controlled manner, the chemical and physical phenomena at the base of this process have not been clarified yet. In this work the attention has been focused on the importance of water transport from the biological wall, simulated by an hydrogel, to the bioadhesive material. Different experiments have been carried out trying to modulate the osmotic pressure of the resulting gel/adhesive material and increase its swelling characteristics.

It has been also studied the effect of the change in water transport, changing the morphology of the gel simulating the biological wall, on the bioadhesive properties. Finally a model has been developed to simulate the water transport, the swelling and the first adhesive elastic response. A good agreement has been found with the experimental data.

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