Theoretical and experimental study of the porous film using quartz crystal microbalance

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The self-assembled multilayers have been studied by many researchers to modify the surfaces of artificial implants for increasing biocompatibility. The accurate mechanical properties of the film can only be obtained from the experimental results using appropriate theoretical models. As the film is composed of both solid polymers and fluid, this paper proposes a two-phase model. Based on the volume average method, the momentum equations are derived for both solid and liquid phases. In order to test our model, we built the porous film on the gold chip of the quartz crystal microbalance using the layer-by-layer method. The buildup process is based on the electrostatic interactions between anionic sodium hyaluronate and cationic chitosan by imitating the endothelial surface layer. By fitting our model to the experimental changes of the resonant frequency and dissipation factor, we get reasonable values of the film thickness, the porosity, the shear modulus of the solid phase, and the permeability. Compared with the existing models, the newly introduced permeability is an important property of the porous layer affecting the values of other parameters. Our model can provide more intrinsic properties of the self-assembled polymeric network and explain its interaction with the permeating fluid. Published by AIP Publishing. [<http://dx.doi.org/10.1063/1.4946876>]

I. INTRODUCTION

For many years, there have been a lot of attempts using artificial implants made of biological materials such as catheters, artificial blood vessels, and vascular stents for treatment of cardiovascular diseases, kidney failure, etc. However, these implants often introduce thrombus, inflammation, and other biocompatible problems. Traditional methods including the use of anticoagulation and antibiotics sometimes do not provide effective results.¹ In order to get blood compatible surfaces, many studies focused on surface modification by imitating the endothelial surface layer (ESL).^{2–10} The ESL is a three dimensional network composed of biomolecules lining the luminal surface of endothelial cells.^{11–13} It is highly hydrated and forms a protective mechanical interface for the blood vessels and prevents adsorption of blood cells and other plasma molecules. There are studies trying to imitate the chemical components or the mechanical structure of this layer. For example, based on the antithrombus property of heparan sulfate, which is an important component of the ESL, the modified surfaces can resist platelet adhesion.^{4,14,15} Some groups modified the implant surfaces with brush-like structures by grafting polymer chains and nanoparticles.^{4,8,9,16} Over the past one or two decades, there emerges an interest in building self-assembled polyelectrolyte multilayers based on polysaccharides using layer-by-layer (LBL) deposition method.^{17–24} The LBL method was first proposed by Kirkland and Iler followed by revitalization and pioneering application of the idea by Decher.²⁵ The multilayers can include many deposition cycles, each of which is composed of two layers of molecules with opposite charges and combined by the electrostatic force.^{26,27} Often glycosaminoglycans, the important components of the ESL, are used as anionic polyelectrolytes because they

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have negatively charged groups like sulfate groups and carboxyl groups. The cationic polyelectrolytes include chitosan and collagen which have positively charged amino groups.

The properties of self-assembled multilayers (SAMs) such as stability, hydrophilicity, and elasticity should reach a certain standard so that the surface modification will work. These properties should be well interpreted by appropriate measuring techniques and theoretical models. As these layers are often built in aqueous solutions, they are the mixtures composed of the solid phase and fluid phase. Traditionally, they are treated as a whole and we can only get the overall film mechanical properties which change with the solid polymer concentration or the porosity. However, this may not be appropriate as these two phases are separated due to the fluid flow and permeation through the solid porous structures. The polymer properties without considering the fluid can provide more intrinsic details. Therefore, it is more reasonable to describe these two phases separately using their own models. Actually, this phenomenon occurs in many fields like underground water flow through rocks and soils^{28–31} and fluid flow in biological tissues.^{32–35} We can use traditional models to describe each phase on the microscopic scale. However, this needs too much computing and is time-consuming in order to get the macroscopic properties. Another approach is the effective models on the macroscopic scale describing average properties of both phases such as the Darcy and Brinkman equations for the fluid³⁶ and the Biot's poroelastic theory for the solid.^{29–31,37}

As for the measuring techniques, the quartz crystal microbalance (QCM) is a very powerful microsensor to characterize film properties.^{38,39} Its main component is a Y-cut piezoelectric quartz crystal plate. An external alternating electric field is applied to the plate through the gold electrodes in order to generate an acoustic wave. As the plate thickness is a half of the wavelength, the plate vibrates in a thickness-shear mode (TSM) and the wave propagates perpendicular to the plate surface. Mass adsorption onto the plate surface will cause changes of the resonant frequency f_n (n is the resonant order and an odd number) and the dissipation factor D . Therefore, QCM can be used to detect physical, chemical, and biological processes on the micro-/nanoscale. There have been some models to interpret the experimental results, such as the Sauerbrey equation for rigid films⁴⁰ and the Kelvin-Voigt model for viscoelastic films.⁴¹ However, these models lack important properties of the porous films such as permeability, porosity, etc. Thus, this paper will build a theoretical model to reinterpret the experimental information and get more intrinsic and useful properties.

II. THE ACOUSTIC WAVE PROPAGATION IN THE POROUS LAYER

The QCM plate vibrating in a TSM mode can be modeled as a simple harmonic oscillator with the same frequency.⁴⁰ But the stored vibrational energy is only a half of that when the whole plate vibrates in a harmonic mode. The schematic model is shown in Figure 1, with the vibrating direction along the x axis. The SAM is treated as a porous layer attached to the plate which will have influence on its vibrating conditions.

The shear stress exerted by the porous layer τ_2 on the QCM plate is proportional to the velocity of the plate surface $\dot{u}_q$, which will be proved later. Here, we define a new parameter ϑ equal to the ratio $\tau_2/\dot{u}_q$. The changes in the resonant frequency and dissipation factor caused by the deposited layer are related to this parameter and written as

FIG. 1. The equivalent harmonic vibration mode of QCM.

$$\begin{aligned}\Delta f &= \text{Im} \left(\frac{\vartheta}{2\pi\rho_q h_q} \right), \\ \Delta D &= -\text{Re} \left(\frac{\vartheta}{\pi f \rho_q h_q} \right),\end{aligned}\quad (1)$$

where ρ_q is the quartz density and h_q is the plate thickness. In the biomechanical field, there appeared many studies on modeling the two-phase mixtures.^{42–46} As the microscopic models have been well studied for each single phase, the volume average method is often used to relate the macroscopic properties with the microscopic ones.^{47–50} For a macroscopically homogeneous and isotropic porous medium, we can choose a representative unit to apply volume averaging. The mixture can be regarded as a continuum containing countless uniform mesoscopic units, which are composed of two microscopically heterogeneous phases. The mesoscopic length scale of each unit volume is much larger than the microscopic scale of each phase while much smaller than the macroscopic scale of the porous system.

For the fluid phase, the momentum equation is $\rho^f \frac{D\mathbf{v}^f}{Dt} = \nabla \cdot \boldsymbol{\sigma}^f$, where ρ^f is the fluid density, $\mathbf{v}^f$ is the fluid velocity, and $\boldsymbol{\sigma}^f$ is the fluid stress tensor. In a unit volume, we can have $\int_V \xi^f (\nabla \cdot \boldsymbol{\sigma}^f) dV = \int_V \nabla \cdot (\xi^f \boldsymbol{\sigma}^f) dV - \mathbf{F}_D$, where $\mathbf{F}_D$ is the total drag force and equal to $\int_{\partial V^f} \mathbf{n}^{sf} \cdot \boldsymbol{\sigma}^f dS$, $\mathbf{n}^{sf}$ is the normal unit vector pointing from solid phase to fluid phase. Here, $\xi^\alpha(\mathbf{x}, t)$ is an indicating function: when the position $\mathbf{x}$ is in α phase, its value is 1; when $\mathbf{x}$ is in β , its value is 0. The stress tensor can be decomposed into two parts, the global part and the local disturbance, as $\boldsymbol{\sigma}^f = \overline{\boldsymbol{\sigma}^f} + \widetilde{\boldsymbol{\sigma}^f}$. For simplification, we can make $\int_V \nabla \cdot (\xi^f \widetilde{\boldsymbol{\sigma}^f}) dV$ to be equal to 0 with Gray's decomposition and $\overline{\boldsymbol{\sigma}^f}$ becomes the intrinsic average $\langle \boldsymbol{\sigma}^f \rangle^f$.⁴⁸ Then, we have $\int_V \nabla \cdot (\xi^f \boldsymbol{\sigma}^f) dV = V^f \nabla \cdot \overline{\boldsymbol{\sigma}^f} + \mathbf{F}_D^f$, where $\mathbf{F}_D^f$ is the global drag force and equal to $\int_{\partial V^f} \mathbf{n}^{sf} \cdot \overline{\boldsymbol{\sigma}^f} dS$. Thus, we can decompose the total drag force into two parts $\mathbf{F}_D = \overline{\mathbf{F}_D^f} + \widetilde{\mathbf{F}_D^f}$, where $\widetilde{\mathbf{F}_D^f}$ is the Stokes drag force and equal to $\int_{\partial V^f} \mathbf{n}^{sf} \cdot \widetilde{\boldsymbol{\sigma}^f} dS$. The global drag force is due to the heterogeneity of the mixture and is equal to $(\phi^s - \phi_A^s) V \nabla \cdot \overline{\boldsymbol{\sigma}^f}$, where ϕ^s and ϕ_A^s are the solid volume concentration and surface fraction of this unit, respectively. Statistically, for a macroscopically homogeneous porous structure, the solid volume and surface fractions are equal to each other. But when it comes to force balance analysis in one unit volume, the difference should be paid attention to. Especially for particle and cylinder cases,^{51–54} as the surface fraction is 0, the total drag force is always bigger than the Stokes drag force and their relationship is $\widetilde{\mathbf{F}_D^f} = \phi^f \mathbf{F}_D^f$ when neglecting the inertial force. If we allocate the Stokes drag force into the unit volume averagely, the Stokes drag density is obtained as $\boldsymbol{\pi}_{sf} = \frac{\widetilde{\mathbf{F}_D^f}}{V}$. The Stokes drag density $\boldsymbol{\pi}_{sf}$ is proportional to the relative intrinsic average velocity between the fluid and solid phases and expressed as $\boldsymbol{\pi}_{sf} = (\phi^f)^2 \mathbf{K}^{-1} \cdot (\langle \mathbf{v}^f \rangle^f - \langle \mathbf{v}^s \rangle^s)$, where $\mathbf{K}$ is the permeability tensor. For isotropic porous media, $\mathbf{K} = K \mathbf{I}$. Then by applying superficial volume averaging to the momentum equation of Newtonian fluid, we can have

$$\phi^f \rho^f \frac{\partial}{\partial t} \langle \mathbf{v}^f \rangle^f = \phi^f \eta \frac{\partial^2}{\partial y^2} \langle \mathbf{v}^f \rangle^f - \frac{\eta (\phi^f)^2}{K} \left(\langle \mathbf{v}^f \rangle^f - \frac{\partial}{\partial t} \langle \mathbf{u}^s \rangle^s \right), \quad (2)$$

where ϕ^f is the porosity. We can do a similar analysis for the solid phase and get the average momentum equation of the linear elastic solid as

$$\phi^s \rho^s \frac{\partial^2}{\partial t^2} \langle \mathbf{u}^s \rangle^s = \phi^s \mu^s \frac{\partial^2}{\partial y^2} \langle \mathbf{u}^s \rangle^s + \frac{\eta (\phi^f)^2}{K} \left(\langle \mathbf{v}^f \rangle^f - \frac{\partial}{\partial t} \langle \mathbf{u}^s \rangle^s \right), \quad (3)$$

where μ^s is the solid shear modulus, and $\langle \mathbf{u}^s \rangle^s$ is the solid intrinsic average displacement.

The momentum transfer at the interface between the porous layer and free layer is important in many fields,^{55–58} such as the benthic boundary layer,⁵⁹ the articular cartilage, and the

synovial fluid.⁶⁰ However, this problem remains unresolved even though there have been a few models proposed, including the Beavers-Joseph condition^{61,62} and the OTW boundary condition.^{63,64} For the QCM case, only the shear stress is transferred. It is certain that all the shear stress of the free fluid is transferred to the porous layer. Then, we can write $\phi^f \frac{\partial}{\partial y} \langle v^f \rangle^f + \phi^s \mu^s \frac{\partial}{\partial y} \langle u^s \rangle^s = \frac{\partial v^b}{\partial y}$ at the interface, where v^b is the velocity of the free fluid. However, we do not know how much the shear stress is partitioned to both phases. We can use a partition parameter χ to count for the partition ratio of the fluid phase as $\phi^f \frac{\partial}{\partial y} \langle v^f \rangle^f = \chi \frac{\partial v^b}{\partial y}$. Minale proposed that χ is equal to the porosity, which is used in this paper.^{65,66} It is obvious that the velocity should be continuous at the interface between the porous layer and free layer: $\phi^f \langle v^f \rangle^f + \phi^s \langle v^s \rangle^s = v^b$.⁶⁰ The velocities of the solid and fluid phases at the plate surface are both equal to the plate velocity.

As shown in Figure 1, the free layer is the background fluid, and its thickness is quite large compared with the porous layer. Then, we may assume h_1 approaches infinity and v^b will reach 0. The velocity of the free layer follows the Stokes equation $\rho^f \frac{\partial v^b}{\partial t} = \eta \frac{\partial^2 v^b}{\partial y^2}$. As the time term is expressed as $e^{i\omega t}$, where ω is the angular frequency, the derivatives with respect to time are $\frac{\partial}{\partial t} \langle v^f \rangle^f = i\omega \langle v^f \rangle^f$, $\frac{\partial}{\partial t} \langle u^s \rangle^s = i\omega \langle u^s \rangle^s$, $\frac{\partial^2}{\partial t^2} \langle u^s \rangle^s = -\omega^2 \langle u^s \rangle^s$, and $\frac{\partial v^b}{\partial t} = i\omega v^b$. The characteristic parameters to nondimensionalize the coordinates and variables are $y = Hy'$, $\langle v^f \rangle^f = \dot{u}_q v^{f'}$, $\langle u^s \rangle^s = \frac{1}{i\omega} \dot{u}_q u^{s'}$, and $v^b = \dot{u}_q v^{b'}$. Here, H can be chosen to be equal to h_2 . By eliminating the solid displacement, the nondimensionalized equation for the velocity of the fluid phase becomes a linear fourth order homogeneous differential equation. Thus, the velocity is expressed as $v^{f'} = \sum_{i=1}^4 c_i e^{\lambda_i y'}$, where $i = 1, 2, 3, 4$, $\lambda_i = \pm \sqrt{\frac{-A_1 \pm \sqrt{A_1^2 + 4A_2}}{2}}$, and $A_1 = \left(\omega^2 \left(\rho^s + \frac{\mu^s}{i\omega\eta} \right) - \frac{\phi^f}{\phi^s} \frac{\phi^f i\omega\eta + \phi^s \mu^s}{K} \right) \frac{H^2}{\mu^s}$, $A_2 = \left(\frac{i\omega\rho^f \rho^s}{\eta} + \frac{\phi^f}{\phi^s} \frac{\phi^s \rho^s + \phi^f \rho^f}{K} \right) \frac{\omega^2 H^4}{\mu^s}$. According to the 4 boundary conditions, we can get the coefficients c_i . Then, we can have the shear stress τ_2 equal to the average stress of the mixture and get ϑ_p

$$\vartheta_p = \left(\frac{\phi^f \eta}{H} + \frac{\phi^s \mu^s}{i\omega H} + \frac{\phi^s \mu^s \rho^f K}{\phi^f \eta H} \right) \sum_{i=1}^4 c_i \lambda_i e^{-\lambda_i h_2} - \frac{\phi^s \mu^s K}{i\omega \phi^f H^3} \sum_{i=1}^4 c_i \lambda_i^3 e^{-\lambda_i h_2}. \quad (4)$$

This shows that the shear stress is actually proportional to the plate velocity. Before the adsorption of SAMs, the free fluid is pumped into the QCM chamber, which also causes changes in the oscillating condition. Therefore, the changes due to the free fluid are usually set to be the baseline. For a Newtonian free fluid, the surface shear stress is expressed as $-\dot{u}_q \sqrt{i\omega\rho^f \eta}$. Then, the actual ϑ parameter that we need to compare with the experimental results is $\vartheta_c = \vartheta_p + \sqrt{i\omega\rho^f \eta}$.

If the mechanical properties of the SAMs are already known, we can get the changes in the resonant frequency and dissipation factors according to Equation (1). However, the fact is that their values are unknown. We need to compare with the experimental results Δf_e and ΔD_e , and then search for the possible values that minimize the error $E^2 = \sum_n \left(\left(\frac{\Delta f_{e|n} - \Delta f_{e|n}}{\Delta f_{e|n}} \right)^2 + \left(\frac{\Delta D_{e|n} - \Delta D_{e|n}}{\Delta D_{e|n}} \right)^2 \right)$, where $n = 1, 3, 5, 7, \dots$. The unknowns may include the film thickness, porosity, solid shear modulus, permeability, etc. Each resonant order can provide two known experimental results, including Δf_e and ΔD_e . We need to make sure that the number of knowns is greater than unknowns.

If the permeability is small enough with the satisfaction of the assumption $\frac{K}{h_2^2} \ll 0$, the drag force will attach the two phases together to be one single viscoelastic solid, which is described by the Kelvin-Voigt model.^{39,41} If the thickness of the film is relatively small, we can further simplify the exponential function to get

$$\vartheta_c = \left(\frac{i\omega\eta\rho^f}{\phi^f i\omega\eta + \phi^s \mu^s} - (\phi^f \rho^f + \phi^s \rho^s) \right) i\omega h_2. \quad (5)$$

Actually, the Kelvin-Voigt model in the literature does not include the porosity or the solid concentration because they are embedded into the shear modulus, viscosity, and densities. Thus, it can only predict the superficial average properties of the porous film, such as the superficial average modulus $\langle \mu^s \rangle = \phi^s \mu^s$. When the porosity is small and the solid shear modulus is quite large, the frequency changes have negative values and the dissipation factor approaches 0, indicating that the adsorbed layer becomes rigid and vibrates along with the QCM plate with little phase difference. This has the effect of increasing the plate mass. Then, we can get $\vartheta_c = -i\omega\rho^s h_2$ and the frequency changes for each order are $\Delta f_n = -\frac{nf_0}{\rho_g h_g} \rho^s h_2$, where f_0 is the fundamental resonant frequency. This is the well-known Sauerbrey equation for the rigid films.⁴⁰

III. EXPERIMENTS

In our experiment, we use the sodium hyaluronate (NaHA) with carboxyl groups ($-\text{COO}^-$) as polyanion and chitosan with amino groups ($-\text{NH}_3^+$) as polycation. NaHA is an important component of the synovial fluid in the articular cartilage and is a great lubricant. NaHA is bought from Acros Organics. Based on the Huggins equation and the Mark-Houwink-Sakurada equation, we measured the viscosity of dilute NaHA solution, and the average molecular weight is about 1.73 MDa.^{67–69} Chitosan is bought from J&K Chemicals with a molecular weight of about 0.2 MDa.

We use 0.1 M acetic acid buffer solution (0.1 M NaCl) with a pH equal to 5.0 as the base solution in order to increase the solubility of chitosan. The concentrations of NaHA and chitosan are both 1 mg/ml. The experiment followed the standard LBL procedure. In between the pumping of the polyelectrolyte solutions which are kept for about 5 to 10 min, the base solution is pumped for 5 min. The QCM version we used is Z500 with the fundamental frequency to be 5 MHz. The quartz crystal plate was immersed in 3 mM MEA (2-mercaptoethylamine hydrochloride) ethanol solution for two days, and MEA molecules are adsorbed onto the plate surface due to the sulfur-gold bond. Then, NaHA can be better adsorbed because of the electrostatic force between the carboxyl groups of NaHA and amino groups of MEA. Finally, we built an eleven-layer film (NaHA/Chitosan)₅NaHA. The fifth order frequency change is shown in Figure 2. With the buildup of the film, the resonant frequency gradually decreases.

IV. DISCUSSION

According to Equation (4) and the experimental results of the first and third order, we obtained the theoretical properties of the porous film. If we assume the density of the fluid phase is 1g/cm^3 , the density of the solid phase is 1.2g/cm^3 , the model predicts that the film thickness is 128 nm, the porosity is 18%, the solid shear modulus is 251 Pa, and the permeability is $1 \times 10^{-14}\text{m}^2$. We can compare these properties of the SAMs with those of the *in vivo* ESL. According to the literature, the porosity of the ESL can be up to 99%.^{35,70} The permeability of the ESL can be as small as $10^{-18} \sim 10^{-17}\text{m}^2$. This comparison indicates that the bionic film has more solid part and larger permeability, thus causing low hydrophilicity and low compactness. As the hyaluronan is the important component of the ESL, the bionic film and ESL

FIG. 2. The fifth order frequency change of QCM caused by the SAM buildup process.

FIG. 3. The influence of film permeability on the changes in the first order frequency and dissipation factor.

should have a similar solid shear modulus. Therefore, we can predict that the superficial average shear modulus of the ESL may be close to 2.51 Pa with the solid concentration to be 1%. This predicted value is larger than the wall shear stress exerted by the blood flow with a typical value of 2 Pa in a 6 μm capillary and smaller than the deforming stress of red blood cells with a typical value of 6 Pa.⁷¹ This explains why the ESL can maintain its shape in blood flow but is crushed by motionless red blood cells in capillaries.⁷²

If we consider the film rigid, we can use the Sauerbrey equation. Using different resonant frequencies, the film thickness has different theoretical values: $H_1 = 118.0 \text{ nm}$, $H_3 = 98.3 \text{ nm}$, $H_5 = 88.5 \text{ nm}$, and $H_7 = 84.3 \text{ nm}$, where the subscripts denote the resonant order. The predicted thickness decreases with the increase in the resonant order, indicating that the rigid assumption is not valid. Our porous model predicts larger thickness than the Sauerbrey prediction. Figure 3 shows the influence of permeability on the changes of the first order frequency and dissipation factor near the best fit theoretical values. The relationship is quite complex. This is why we need more experimental data to fit for the best values of mechanical properties. When the permeability is around 10^{-14} m^2 , both the changes in the frequency and dissipation factors fluctuate a lot because the ratio K/H^2 is close to 1. When the permeability decreases, the curves gradually become smooth, indicating that the porous layer may be considered as a viscoelastic layer. However, the frequency change becomes positive because of the small shear modulus. The Kelvin-Voigt model will predict higher shear modulus in order to satisfy the negative frequency change. It is noteworthy that the comparison with only the four experimental dissipation factors predicts a much larger shear modulus to be around $3.16 \times 10^5 \text{ Pa}$ and a much smaller permeability to be about $7.94 \times 10^{-16} \text{ m}^2$. But these predicted values cannot satisfy the frequency changes at the same time. Actually, the theoretical prediction really depends on the accuracy of the experimental results, which needs more study in the future. Therefore, the permeability has a great influence on the drag force between the fluid and solid phases, causing the changes in other parameters.

V. CONCLUSIONS

Due to the demand of appropriate models in the analysis of mechanical properties of self-assembled multilayers, this paper proposes a two-phase model by treating the films as porous media. The momentum equations for the solid and fluid phases are derived based on the volume average method. Then, we apply the porous model for the measurement of adsorbed films onto the plate of quartz crystal microbalance which is a widely used microsensor for adsorption and detection in many nano/micro-fields. Our porous model can reduce to the Kelvin-Voigt model with the assumption of low permeability and then reduce to the Sauerbrey equation for rigid films with infinite shear modulus and zero porosity. We did a simple experiment using the layer-by-layer method to build a porous film onto the quartz crystal plate. By fitting our model to the experimental changes in the resonant frequency and dissipation factor, we obtained reasonable values of the film thickness, the porosity, the solid shear modulus, and the permeability. The film's thickness is larger than the Sauerbrey prediction because of its finite shear modulus.

The permeability should not be neglected as it has important influence on the experimental results, especially when it is of the same order of the square of the film thickness. Compared with the actual endothelial surface layer, the bionic film properties are far from perfect. Higher compactness and hydrophilicity are needed for better surface modification.

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