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Research paper

# Loading velocity dependent permeability in agarose gel under compression

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ABSTRACT

A new approach for characterization of agarose gel permeability under compression at different loading velocities is proposed. Uniaxial compression tests on thin agarose gel specimens in a rigid porous confinement cell immersed in a water bath are undertaken. The equilibrium response of the gel, which is assumed to be achieved under extremely low-loading velocity (of the order of tens nanometers per second) is considered to be the response of the hydrated gel scaffold. The water exudation behavior from the agarose gel was extracted from the load–displacement response under various loading velocities by subtracting the equilibrium response. It was found that the pressure on water in the gel is not a linear function of loading velocity or volume flow rate and therefore, the permeability of agarose gel was observed to vary with deformation and water flow velocity. In addition, it was inferred from the analysis that at low velocities and large strain levels the gel permeability dominates the compression behavior, and at higher velocities and small strain levels the viscosity of the hydrated matrix may contribute to the load. Finally, permeability variation in agarose gel at different loading velocities is attributed to the two states (free water and bound water) of water molecules in the gel.



## 1. Introduction

Agarose gel is traditionally used as a medium in electrophoresis and also as a phantom material or tissue scaffold in biomedical engineering. Understanding its mechanical behavior is essential for effective use as a tissue surrogate under complex loading conditions. Extensive research has been conducted on its wide range of mechanical properties including dynamic stiffness (Benkherourou et al., 1999; Chen et al., 2005; De Freitas et al., 2006; Miyata et al., 2008), effect of molecular weight on failure stress and strain in tension and compression (Normand et al., 2000), stress relaxation behavior (Nussinovitch et al., 1989; Mauck et al., 2000), and hydraulic permeability (Lai and Mow, 1980; Jackson and James, 1986; Holmes and Mow, 1990; Johnson and Deen, 1996; Zhang et al., 2000; Andarawis et al., 2001; Yao and Gu, 2002; Gu et al., 2003; O'Brien et al., 2007). Because agarose is a biopolymer with a range of molecular weights, property variations in agarose gels may arise from a wide variety of sources including some intrinsic factors such as agarose concentration, type of agarose and its molecular structure, and molecular

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weight, as well as some extrinsic factors such as its preparation method and thermal history (Aymard et al., 2001; Buckley et al., 2009).

Similar to many other biopolymers or biological tissues, agarose gel shows considerable stress relaxation and/or strain-creep behavior in ambient temperature. The mechanism behind stress relaxation and strain-creep in agarose gel is completely different from that in traditional engineering materials: water redistribution and exudation play an important role, or may dominate the relaxation and/or creep phenomenon in gel; while for traditional engineering structural materials, constituent redistribution and mass loss are negligible. Because water redistribution in agarose gel (or other similar biphasic materials) under deformation/stress is governed by its hydraulic permeability (or conductivity), researchers have focused their effort on understanding the permeability. Mow et al. (1980) presented theoretical analysis for creep and relaxation based on a biphasic model in which the solid matrix was treated as linear elastic material and the assumption of incompressibility for solid matrix and interstitial fluid was invoked. The assumption of incompressibility implied that the relaxation at a specific deformation was solely caused by redistribution of water in the material. Nonlinear dependence of permeability on deformation was presented later by Lai et al. (1981). Johnson and Deen (1996) proposed a direct method to measure gel permeability. Gu et al. (2003) provided further insight into the deformation-dependent permeability of agarose gel in which the current (evolving) water/solid volume fraction was used to determine permeability based on the biphasic model proposed by Mow et al. (1980).

The constituents of gel consist of two parts: (i) an agarose scaffold (matrix) and (ii) water. As early as 1973, Jhon and Andrade (1973) proposed a material model for water in a hydrogel. The water was classified into three states: free water, bound water and intermediate water. Free water refers to those water molecules which may move as soon as a load is applied. The bound water includes those water molecules which adhere to the solid gel matrix via hydrogen-bond. Intermediate water is in a transition state between free water and bound water. The hydrogen-bond between water molecules and other hydrophilic matrix molecules was later verified via nuclear magnetic resonance (NMR) technique (Katayama and Fujiwara, 1980; Nagura et al., 1996; Ghi et al., 2002; McConville et al., 2002; Morita et al., 2007) and Raman spectra analysis (Terada et al., 1993; Kitano et al., 2005; Li et al., 2004; Gadomski and Ratajska-Gadomska, 2004; Ratajska-Gadomska and Gadomski, 2004). Utilizing lattice spin relaxation time, McConville et al. (2002) determined the activation energy with respect to water content in various hydrogels. It was clearly shown that activation energy increased as the overall water content decreased, i.e., the mobility of water molecules was reduced. Even though it is clear that some molecular mechanism should be responsible for the macroscopic mechanical behavior, there is no simple quantitative correlation between the spectroscopy (NMR or Raman) and mobility of water.

Gels are used as surrogates for cartilage and as artificial tissue scaffold for brain tissue, and therefore, understanding of the mass transport through gels is required. Knowledge on gel permeability and its variation under different loading conditions is essential for modeling its mechanical response and extrapolating its behavior in more complex scenarios. Modeling approaches that capture the fundamental permeability behavior of gels exhibited in simple experiments are necessary in this endeavor. In this work, agarose gel was deformed at various loading velocities under uniaxial compression in a porous confinement cell immersed in a water bath. At extremely low loading velocity (on the order of tens of nanometers per second), the stress–strain response is assumed to reach an equilibrium condition, in which the stress is carried solely by the hydrated scaffold and the fluid remains at rest (no motion). A new approach is presented to systematically characterize water exudation behavior of agarose gel under compression. Contrary to the traditional concept of permeability which is an intrinsic property of a porous medium and remains constant under different fluid velocities, the permeability variation of agarose gel with respect to fluid flow velocity in addition to magnitude of deformation is suggested.

## 2. Material and method

DNA analysis-grade agarose powder from Fisher Scientific (www.fishersci.com) was used to prepare agarose gel with concentration at 2.4% (w/w) by adopting the following procedure. A specified amount of agarose powder was added to a beaker as per the intended concentration and desired final solution mass. Cold deionized water was added into the beaker and the cold mixture was heated in a microwave oven and stirred intermittently. When the solution began to boil, the beaker was moved into a pressure cooker with boiling water. After around 10–15 min, the solution became clear and bubble free and was poured into a pre-heated plastic mold. The plastic mold consists of a thin plastic sheet (1.48 mm thick) with holes of diameter 22.23 mm. The sheet is supported on a thick plastic panel at the bottom. Both these plastic parts are fastened together using plastic bars on top and bottom. The prepared solution was poured into the mold holes, and the surplus solution was forced out of the mold by covering the filled holes with additional plastic bars. Upon curing at room temperature for 45–60 min, the mold was disassembled and the cast gel specimens of diameter 22.23 mm and thickness 1.48 mm were removed and placed in a water bath to prevent dehydration. The specimen was intentionally made thin to facilitate quick exudation of water under load so as to reach equilibrium. A thick gel specimen was avoided in our experiment because upon deformation, the interior portion of the gel specimen would require an extended period of time to exude water and reach equilibrium.

An MTS Alliance R/T 30 test machine with 100 N load-cell was used for uniaxial compression test. A range of crosshead velocities from 0.00005 to 0.5 mm/s were used (covering 4 orders of magnitude) to deform the gel specimens. The tests at lower loading velocity range were intended to examine the equilibrium response and those at higher loading velocity range were intended to investigate water exudation behavior from the gel specimen. Five specimens were tested at each selected crosshead velocity. Fig. 1 shows the schematic of