Designation: F2952 – 22

Standard Guide for Determining the Mean Darcy Permeability Coefficient for a Porous Tissue Scaffold[1]

This standard is issued under the fixed designation F2952; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide describes test methods suitable for determining the mean Darcy permeability coefficient for a porous tissue scaffold, which is a measure of the rate at which a fluid, typically air or water, flows through it in response to an applied pressure gradient. This information can be used to optimize the structure of tissue scaffolds, to develop a consistent manufacturing process, and for quality assurance purposes.

1.2 The method is generally nondestructive and noncontaminating.

1.3 The method is not suitable for structures that are easily deformed or damaged. Some experimentation is usually required to assess the suitability of permeability testing for a particular material/structure and to optimize the experimental conditions.

1.4 Measures of permeability should not be considered as definitive metrics of the structure of porous tissue scaffolds and should complement measures obtained by other investigative techniques, for example, scanning electron microscopy, gas flow porometry, and micro-computer X-ray tomography (Guides F2450, F2603, and F3259).

1.5 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.6 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D737 Test Method for Air Permeability of Textile Fabrics
D2434 Test Methods for Measurement of Hydraulic Conductivity of Coarse-Grained Soils
F2450 Guide for Assessing Microstructure of Polymeric Scaffolds for Use in Tissue-Engineered Medical Products
F2603 Guide for Interpreting Images of Polymeric Tissue Scaffolds
F3259 Guide for Micro-computed Tomography of Tissue Engineered Scaffolds
F3510 Guide for Characterizing Fiber-Based Constructs for Tissue-Engineered Medical Products

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *tortuosity, n*—the ratio of the actual path length through connected pores to the Euclidean distance (shortest linear distance).

4. Significance and Use

4.1 This document describes the basic principles that need to be followed to obtain a mean value of the Darcy permeability coefficient for structures that consist of a series of interconnected voids or pores. The coefficient is a measure of the permeability of the structure to fluid flowing through it that is driven by a pressure gradient created across it.

4.2 The technique is not sensitive to the presence of closed or blind-end pores (Fig. 1).

4.3 Values of the permeability coefficient can be used to compare the consistency of manufactured samples or to determine what the effect of changing one or more manufacturing settings has on permeability. They can also be used to assess the homogeneity and anisotropy of tissue scaffolds. Variability in the permeability coefficient can be also be indicative of:

4.3.1 Internal damage within the sample, for example, cracking or permanent deformation.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

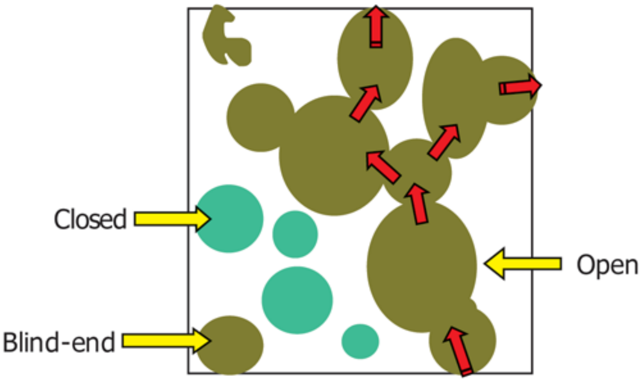

FIG. 1 Schematic of the Different Pores Types Found in Tissue Scaffolds. Fluid Flow Through the Structure is via the Open Pores

4.3.2 The presence of large voids, including trapped air bubbles, within the structure.

4.3.3 Surface effects such as a skin formed during manufacture.

4.3.4 Variable sample geometry.

4.4 This test method is based on the assumption that the flow rate through a given sample subjected to an applied pressure gradient is constant with time.

NOTE 1—If a steady-state flow condition isn't reached, then this could be due to structural damage (that is, crack formation or the porous structure deformed as a result of the force being placed upon it by the fluid flowing through it). Sample deformation in the form of stretching (bowing) can also occur for less resilient structures as a result of high fluid flow rates. This topic is discussed in more detail in Section 7.

4.5 Care should be taken to ensure that hydrophobic materials are fully wetted out when using water or other aqueous-based liquids as permeants.

4.6 Conventionally, the pressure differential created across a sample is measured as a function of both increasing and decreasing flow rates. An alternative approach, which may be practically easier to create, is to apply a range of different pressure differentials across the sample and measure the resultant flow of fluid through it. The hysteresis that occurs during a complete cycle of increasing flow rate followed by a progressive decrease in flow rate can provide an excellent measure of the behavioural consistency of the matrix. Significant hysteresis in the measured pressure differential during increasing and decreasing flow rates can indicate the existence of induced damage in the structure, the fact that the material is behaving viscoelastically, or is suffering from permanent plastic deformation. Some guidance on how to identify which of these factors is responsible for hysteresis is provided in Section 7.

4.7 It is assumed that Darcy's law is valid. This can be established by plotting the volume flow through the specimen against the differential pressure drop across the specimen. This plot should be linear for Darcy's law to apply and a least-squares fit to the data should pass through the origin. It is not uncommon for such plots to be nonlinear which may indicate that the structure does not obey Darcy's law or that the range of pressures applied is too broad. This topic is further discussed in Section 7.

5. Characterization and the Structural Features of Tissue Scaffolds

5.1 Porous tissue scaffolds are typically manufactured from polymers and ceramics and consist of a network of connected voids through which cells, macromolecules such as growth factors, and small molecules such as nutrients and dissolved gases can move (**1**).[3] The material used to create the scaffold may disappear over time, either as a result of enzyme activity or some other degradation processes (for example, hydrolysis). The time-dependent permeability of tissue scaffolds to dissolved gases and solutes is critical to their function, particularly for high levels of cell occupancy due to the demands for oxygen and nutrients as well as the need to remove waste products.

5.2 There are many methods available for characterizing the structural features of scaffolds (Guides F2450 and F3510), but these can be time consuming, expensive to use, and can result in permanent damage or contamination to the scaffold.

5.3 Most investigators report some measure of pore size and an estimate of the scaffold porosity (**2, 3**). However, there are significant practical issues associated with these measurements. Techniques such as mercury porosimetry and gas flow porometry are used to estimate pore size distributions which typically differ by an order of magnitude due to differences in the underlying physics of the techniques (Guide F2450). Despite the shortfalls of these techniques, both can be used to infer a useful amount of information regarding the structure of the scaffold. Both porosimetry and porometry represent the scaffold structure as a distribution of differently sized parallel-sided pores, that is, the model assumes a simple structure that is equivalent to the more complicated structures usually manufactured where the pores are not parallel-sided and not of uniform diameter.

5.4 Electron and other microscopies are extensively used to image scaffolds, but the data that these techniques produce is often challenging to interpret without some undefinable level of uncertainty (that is, quantifying the dimensions of typically

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[3] The boldface numbers in parentheses refer to the list of references at the end of this standard.

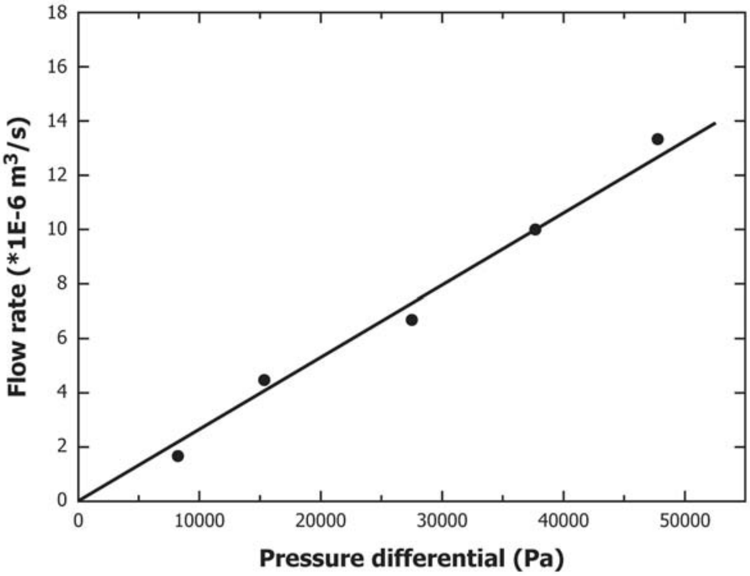

FIG. 2 Example of a Plot of Flow Rate versus Pressure Differential

irregularly shaped and sized structural features). The same arguments apply to tomographic methods such as magnetic resonance imaging and micro-computer tomography (µCT); for example, calculations based on the analysis of a series of scaffold images obtained from a tomographical method such as µCT will depend on how well the boundaries of the voids or pores can be defined, on the instrument resolution in the *x*, *y* and *z* planes, and the methodology used to obtain dimensional information (Guide F3259). Nevertheless, many groups have pursued quantitative analysis of pore size distributions in polymeric (**3**) and bioceramic (**4**) matrices in recognition of the important correlation between this parameter and tissue in-growth.

5.5 The pores in a tissue scaffold typically consist of a series of irregularly shaped voids[4] that can be connected to each other both by partial fusion and connecting channels (connects). Through pores provide a path through the scaffold from one side to the other (see Fig. 1), and are the primary routes for fluid penetration into the scaffold. The dimensions of a given pore can be difficult to define due to, for example, merging of adjacent cavities that result in fenestrations or "windows" forming in the void walls. Blind-end and closed-pores, although not contributing to measures of fluid permeability, play an important role in gas diffusion through the structure.

6. The Darcy Permeability Coefficient

6.1 The Darcy permeability coefficient is a measure of the resistance of a porous material to flow of a fluid through it that is governed by the dimensions and density of open (or through) pores and by the tortuosity of the structure.

6.2 In its simplest form, the permeability coefficient, *k*, of the scaffold can be determined by measuring the flow of fluid through the material in a given time under a known pressure gradient using Darcy's law (**5**), that is,

$$Q = \frac{-kA(P_b - P_a)}{\mu L} \quad (1)$$

which states that the flow rate (Q, (m^3/s)) through the material is directly proportional to the cross-sectional area (A, (m^2)) and the pressure drop ($P_b - P_a$, (Pa)) and inversely proportional to the viscosity of fluid (μ, (Pa.s)) and the length (L, (m)) over which the pressure drop occurs.

6.3 The permeability coefficient, *k*, is then derived from the slope of a linear plot of flow rate versus pressure drop where the slope is forced to pass through the origin (see Fig. 2).

6.4 The SI units of the coefficient are m^2.

6.5 Permeability coefficients are used in assessing soils, filters, and other porous materials (Test Methods D737 and D2434) and have also been used to characterize polymeric scaffolds and hard tissues, for example, cancellous bone (**6-11**).

7. Methodology

7.1 Obtaining reliable values for the permeability coefficient involves a degree of experimental optimization to ensure that a range of flow rates and pressure differentials can be measured. Clearly, it is advantageous to measure a range of flow rates and pressure differentials to improve the reliability of the Darcy coefficient, but this can produce nonlinear plots for reasons that are discussed in Section 8. This will require some experimentation to optimize the sample geometry and to select the most appropriate fluid, typically air or water, for a given structure/sample geometry and material type. Subsections 7.3 and 7.4 describe the features that are required in an experimental system in order to obtain robust estimates of the coefficient.

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[4] The terminology for scaffold structure is not well defined. The term "pore" is widely used to mean a void, a window in a void, or a conduit connecting two or more voids together.

7.2 Reliably determining the pressure differential across the scaffold and measuring the flow rate through it are fundamental aspects of permeability testing. In practice, the sensitivity of the apparatus used to measure pressure will limit the magnitude of the pressure gradient that can be used for a given sample geometry.

7.3 *Gas-Based Systems:*

7.3.1 Fig. 3 shows a schematic representation of apparatus that can be used to measure the flow of gas, in this case compressed air, through a disc-like sample mounted in a commercially available filter holder that can be purchased in a range of sizes.

7.3.2 The rate of flow through the sample is measured by a gas flow meter. These devices are commercially available for different ranges of flow rate. Care should be taken to ensure that the flow meter used is appropriate for the flow rates used to avoid potential measurement inaccuracies. The pressure upstream of the sample, P_b, is measured and used together with a measured value for atmospheric pressure (P_a) to determine the pressure gradient ($P_b - P_a$) required by Eq 1.

7.4 *Liquid-Based Systems:*

7.4.1 Fig. 4 shows an experimental configuration that measures the flow of a liquid, such as water, through a porous tubular scaffold sample. The apparatus consists of a circulating pump, which is used to generate an internal pressure within the circuit (P_b). P_a is the measured value of atmospheric pressure. The internal pressure that develops within the circuit is very dependent on the permeability of the scaffold and its geometry, but is usually sufficiently high that any changes in pressure along the length of a vertically mounted sample due to differences in height can be ignored. However, the user is advised to check that this assumption is valid for the sample and sample geometry that is being investigated.

7.4.2 The water that flows through the walls of the specimen and out through the overflow is collected at given time intervals, weighed, and converted into a flow rate. The fluid reservoir replenishes the fluid lost from the system via the overflow.

7.4.3 Alternative sample geometries can be used (that is, a disc of material sandwiched between O-rings in a commercially available filter holder), as used for gas-based systems. In both cases the practical considerations are the same: how to apply a progressively increasing pressure gradient without significantly deforming the sample or letting fluid flow around it.

8. Practical Considerations

8.1 There are many experimental configurations that can be used to generate the flow rate and pressure differential measurements required to determine Darcy's permeability coefficient. It is not uncommon to observe a degree of nonlinearity in plots of flow rate versus differential pressure, particularly when investigating a new sample, whether it is manufactured from a different material or produced using different processing conditions. The following considerations should be taken into account in designing the apparatus and defining the sample geometry to ensure that the relationship between flow rate and differential pressure is attributed to the structure and not an experimental artifact.

8.2 *Sample Characteristics:*

8.2.1 The samples will need to have sufficient stiffness to ensure that they are able to withstand a pressure gradient without incurring damage or deforming significantly, for example, bowing. Unfortunately the suitability of permeability testing as an experimental method for a given material/structure/sample geometry will need to be established by experimentation using the guidance given in Table 1.

8.2.2 It is recommended that measurements of flow rate and pressure differential be made cyclically to assess potential hysteresis of the system. This can be the simple approach of measuring the flow rates at increasing pressure differentials followed by a progressive decrease back to the start point. A time lag should be allowed before a measurement is made at a given pressure differential to allow the experimental system to reach a steady-state condition.

8.2.3 A significant difference in flow rate after one or more cycles of pressurizing/depressurizing the sample is indicative of a structural change having occurred within a sample. This may be due to viscoelastic effects in a polymer-based scaffold, or may be indicative of either structural damage or permanent plastic deformation. Differentiating between potentially permanent changes in the sample structure from viscoelastic effects is

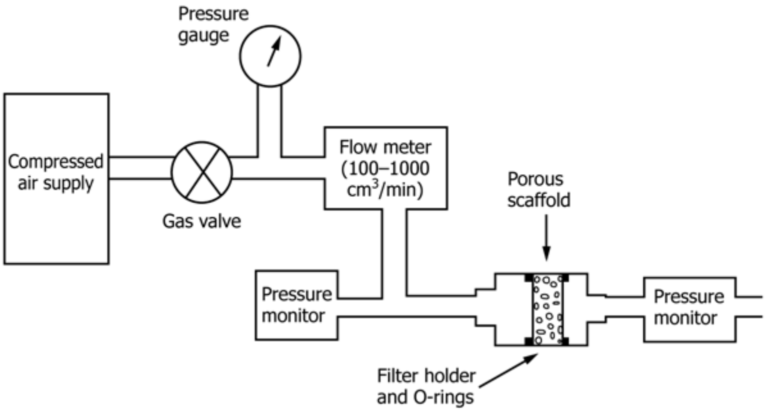

FIG. 3 Measuring the Pressure Differential Across a Disc of a Porous Scaffold Produced by the Controlled Flow of Gas Through the Disc