IMPROVED FILTRATION MEMBRANE AND METHODS OF MAKING AND USING THE SAME

CROSS-REFERENCE

This application claims the benefit of U.S. Provisional Patent Application No. 63/063,038, filed August 7, 2020, and U.S. Provisional Patent Application No. 63/070,999, filed August 27, 2020, which applications are incorporated herein by reference in their entirety

INTRODUCTION

Chronic kidney failure afflicts over 2 million patients worldwide [1]. Current treatment options are dialysis and organ transplant. While kidney transplant provides the best clinical outcomes, the severe shortage of donor organs often forces kidney patients to remain on dialysis for an extended period of time (on the order of years), contributing to a poor quality of life and an increased mortality rate. In addition, regular trips to dialysis centers and undesirable buildup of urea and other toxins in the bloodstream between dialysis sessions tend to adversely affect patients' overall wellbeing [2-4]. It would be of great benefit to have a compact, portable, mass-producible, and ultimately implantable "bio-artificial kidney" that could perform the most critical renal functions.

The major limitations of dialysis treatment and limited availability of organs for kidney transplant have led to a growing interest in alternative renal replacement therapies. Current approaches in development include cell-based strategies, which aim to create a fully functional replacement organ [5-6]; wearable artificial kidney devices based on dialysis technology, which allow patients to receive prolonged and frequent treatments outside of the clinical setting [7-8]; and bio-hybrid devices that attempt to mimic key functions of the native nephron [9-10].

Fundamental to achieving such alternate renal replacement therapies is development of a filtration membrane of submicron thickness that is resistant to breakage but provides sufficient filtration surface. The present disclosure addresses these and other needs.

SUMMARY

According to a first aspect of the present disclosure, there is provided a filtration

membrane suitable for filtering blood in vivo, the filtration membrane comprising: a membrane section comprising: a plurality of nanopores, wherein the plurality of nanopores have at least one lateral dimension in the range of 1 nm to 1000 nm; a planar first surface; a ribbed second surface, wherein the planar first surface is opposite the ribbed second surface, the ribbed second surface comprising ribs of a first height and ribs of a second height which is higher than the first height, wherein the ribs of the second height range in height from 20 μm to 100 μm and in thickness from 1 μm to 20 μm; the ribs of the first height defining a plurality of first windows arranged in a grid pattern, the first windows comprising the plurality of nanopores; the ribs of the second height defining a plurality of second windows arranged in a grid pattern, each of the plurality of second windows comprising the plurality of first windows; and a support section forming a third window comprising the plurality of second windows, wherein the support section is attached to the ribbed second surface of the membrane section at a periphery of the membrane section and has a third height higher than the ribs of the second height, wherein the surface area of the second surface of the membrane enclosed by the third window is in the range of 0.1 mm^2-10 mm^2.

According to a second aspect of the present disclosure, there is provided a method for generating a biocompatible filtration membrane suitable for filtering blood in vivo, the method comprising: depositing a first mask in a first pattern on a first surface of a support substrate, wherein the first pattern exposes areas on the first surface which areas define outlines of a plurality of first rectangles arranged in a grid pattern and a plurality of second rectangles arranged in a grid pattern, wherein the each of the plurality of second rectangles comprise the plurality of first rectangles; depositing a second mask on the first mask such that the second mask covers the exposed areas on the first surface which areas define outlines of the first rectangular windows and does not cover the exposed areas on the first surface which areas define outlines of the second rectangular windows thereby allowing etching of the first surface to create grooves in the support substrate corresponding to the outlines of the second rectangular windows; etching the first surface to create the grooves, the grooves having a depth and a thickness; removing the second mask, wherein the removing the second mask exposes areas on the first surface defining outlines of the plurality of first rectangles; etching the first surface to increase the depth of the grooves of the plurality of the second rectangles and to create the grooves in the support substrate corresponding to the outlines of the plurality of the first rectangles such that the depth of the grooves for the second rectangles is more than that of the first rectangles; removing the first mask; depositing an intermediate layer over the support substrate; depositing a membrane material to fill the grooves of the first and second rectangles created in the support substrate to create a membrane comprising a planar first surface and a non-planar second surface opposite the first

surface, the non-planar second surface comprising a plurality of ribs having a first height corresponding to the depth of the grooves for the first rectangles and a plurality of ribs having a second height corresponding to the depth of the grooves for the second rectangles, wherein the second height is higher than the first height; creating a pattern of fine grooves in regions of the membrane; depositing a sacrificial layer on the membrane; filling the fine grooves with additional membrane material; removing excess additional membrane material not deposited in the fine grooves; removing sacrificial layer from the membrane; removing the intermediate layer and forming a cavity in the second surface of the support structure, wherein the second surface is opposite the first surface to provide: a plurality of nanopores in the membrane, wherein the plurality of nanopores have at least one lateral dimension in the range of 1 nm to 1000 nm, a plurality of first windows defined by the plurality of ribs having the first height, a plurality of second windows defined by the plurality of ribs having the second height, wherein the ribs having the second height range in height from 20 μm to 100 μm and in thickness from 1 μm to 20 μm, wherein each of the plurality of second windows comprise the plurality of first windows, and a third window having a third height defined by the support structure and formed by the walls of the cavity, wherein the third height is higher than the second height and wherein the third window comprises the plurality of second windows.

Embodiments of the present disclosure can provide an improved filtration membrane suitable for filtration of blood *in vivo*. The improved filtration membrane may be resistant to breakage with minimal areal penalty due to presence of a system of supports on the backside of the membrane. The minimal areal penalty is achieved by using supports that provide a hierarchical scaffolding that comprises ribs