Figure 1

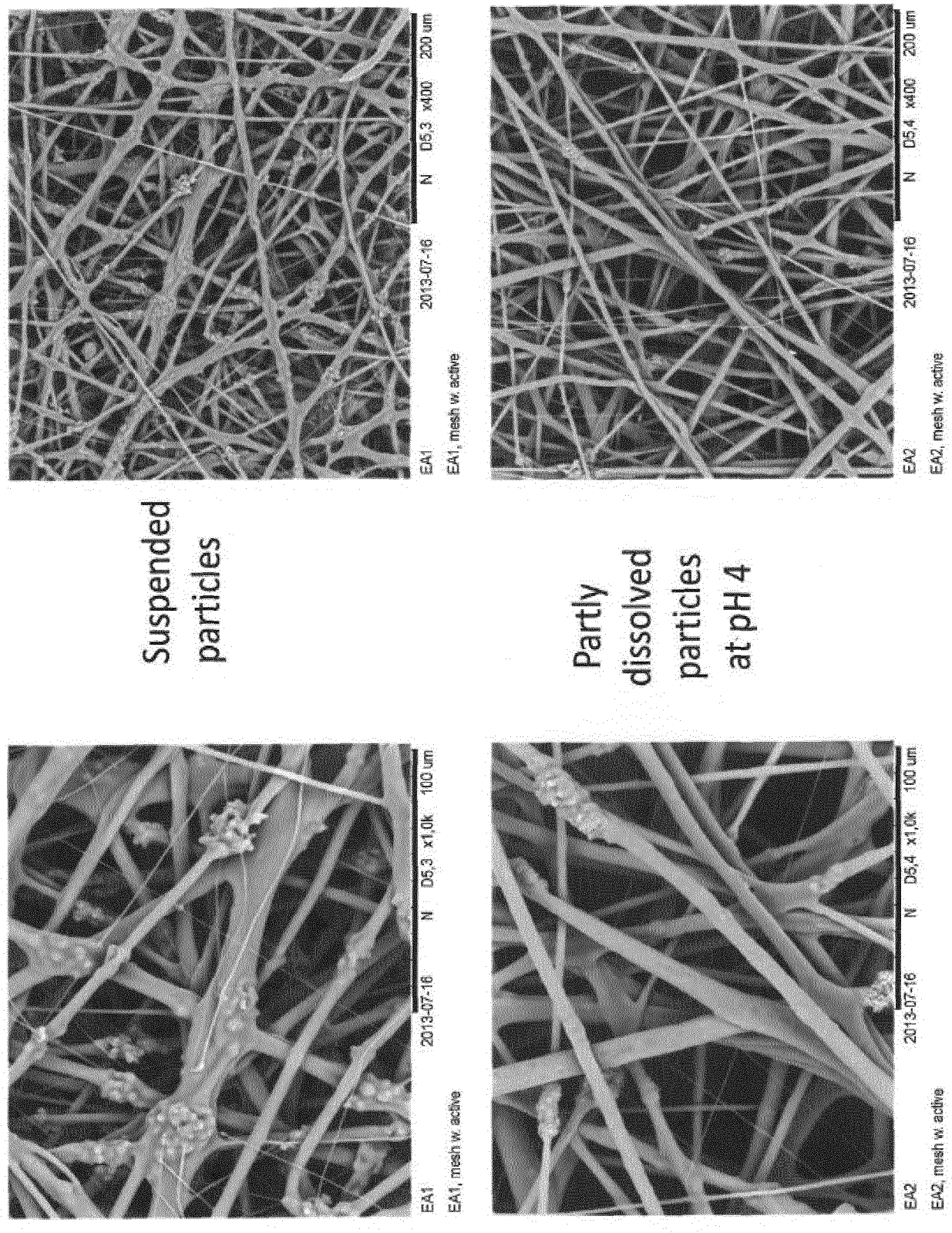

Suspended particles
Partly dissolved particles at pH 4
EA1
EA1, mesh w. active
2013-07-16
N
D5,3
x400
200 um
EA2
EA2, mesh w. active
D5,4
x1,0k
100 um

Figure 2

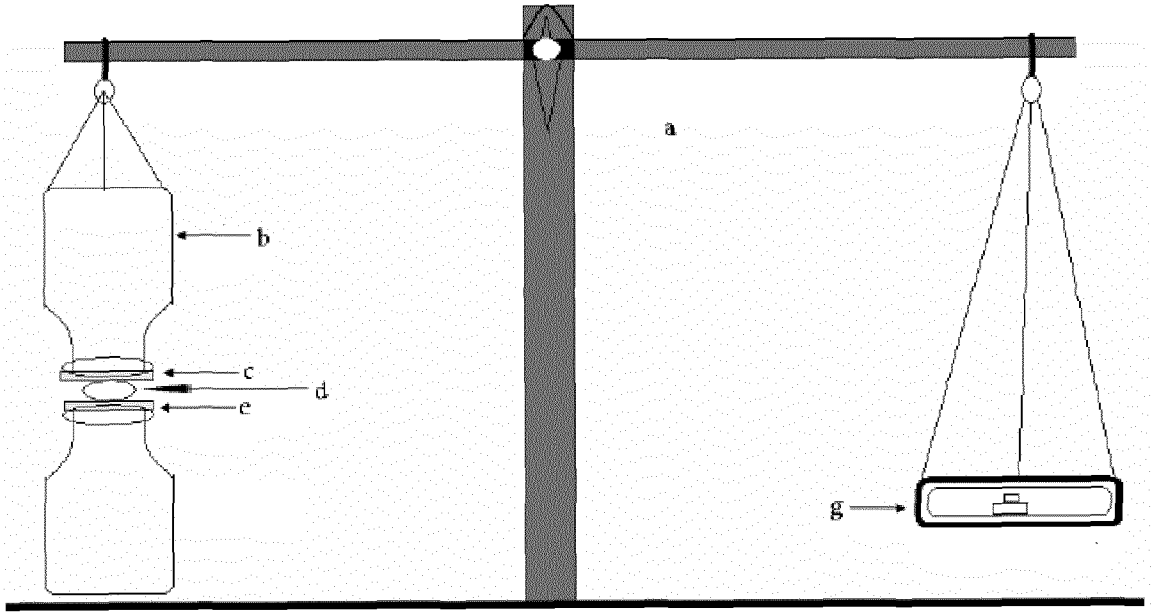


Figure 3

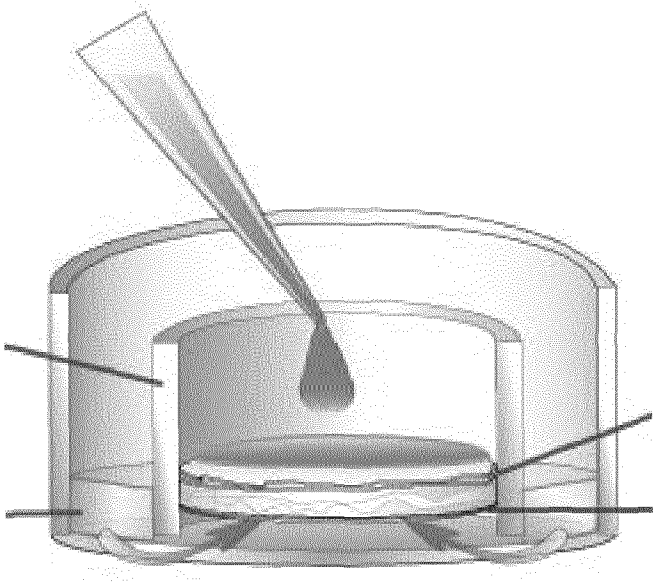

Cell culture insert
Media
Buccal human keratinocytes differentiated morphology with barrier function
Microporous membrane

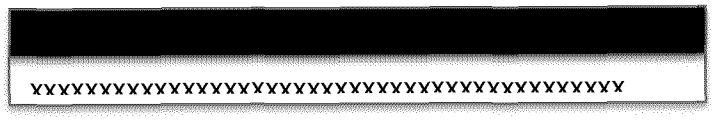
Figure 4

Different release geometry from different sheets



Drug + Bioadhesive + Hydrophilic polymer

Conventional sheet – Bidirectional drug release



Water-impermeable spun or coating

Drug + Bioadhesive + Hydrophilic polymer

Bilayer sheet – Undirectional drug release



Water-impermeable spun or coating

Drug + Hydrophilic polymer

Bioadhesive layer

Triple sheet – unidirectional drug release



Drug + Hydrophilic polymer

Bioadhesive layer

Bilayer sheet – Bidirectional release

Figure 5

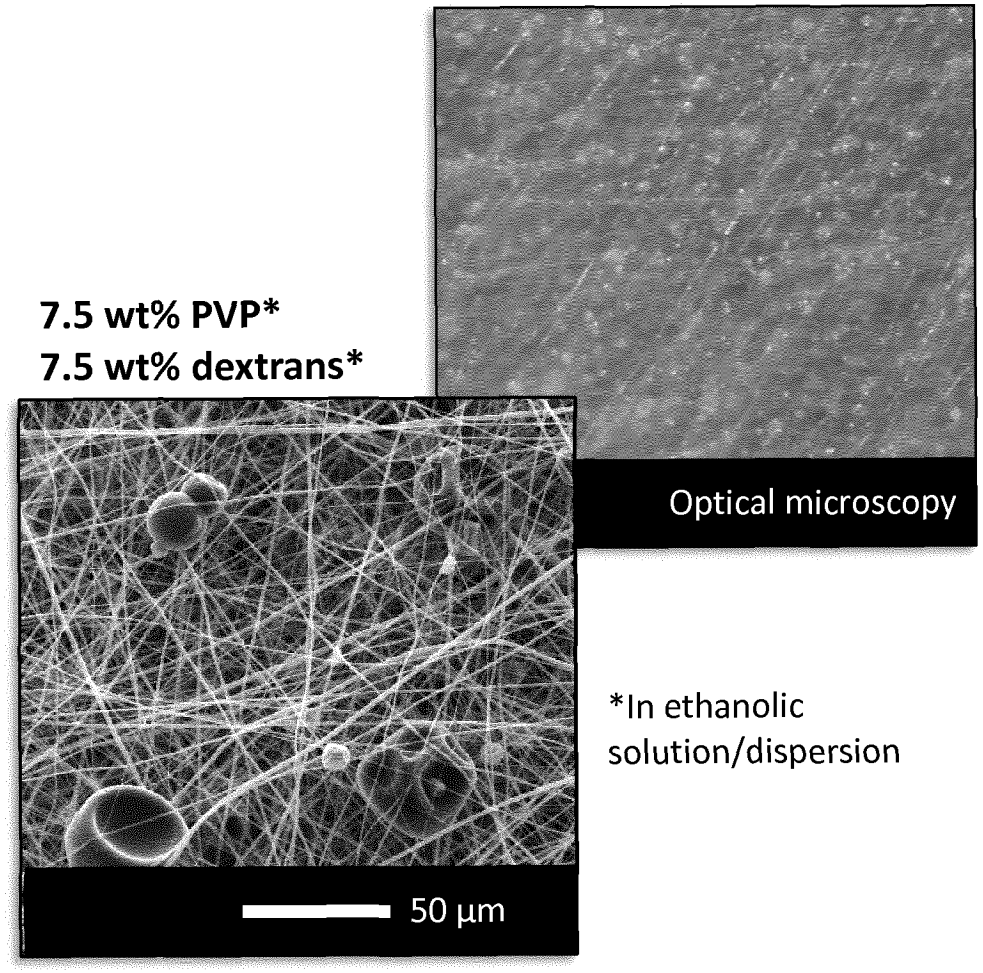
Fabrication of drug-delivery layer
Optimisation of electrospinning method
Manufacturing method
Based on protocol:
10 wt% PVP (Kollidon 90F, BASF) in ethanol
Solution volume = 2 mL
Distance = 17 cm
Voltage = 14 kV
Flow rate = 10 ml h-1
20 gauge needle
Ambient temperature and
10 wt% PVP
50 µm

Figure 6

Fabrication of drug-delivery layer

Addition of dextrans to composition

- 0-15 wt% of dextrans added to PVP solution
- Various Mw
  - ✓T500 = 500,000
  - ✓T2000 = 2,000,000
  - ✓Mixture of both
- Variable particle size
  - ✓<45 µm particle size



*In ethanolic solution/dispersion

Figure 7

Fabrication of drug-delivery layer

Fabrication of dyed materials

- Alcian blue 8GX (Merck)
  - ✓ To observe gel in bioadhesion studies
  - ✓ Powdered
  - ✓ Dissolves in ethanol
- Demonstrates potential of electrospun materials to encapsulate and deliver dissolved substances
  - ✓ Ethanol-soluble drugs

10 wt% PVP + 1 w/v % alcian blue in ethanol solution

Figure 8

Fabrication of drug-delivery layer

Solubility of electrospun materials

- Fast dissolution of PVP in water
  - ✓ < 1 second
- Gel with bioadhesive properties
- Rapid drug release

Solubility test on artifical saliva

Bioadhesiveness test of PVP/PCL on pig mucosa

Figure 9

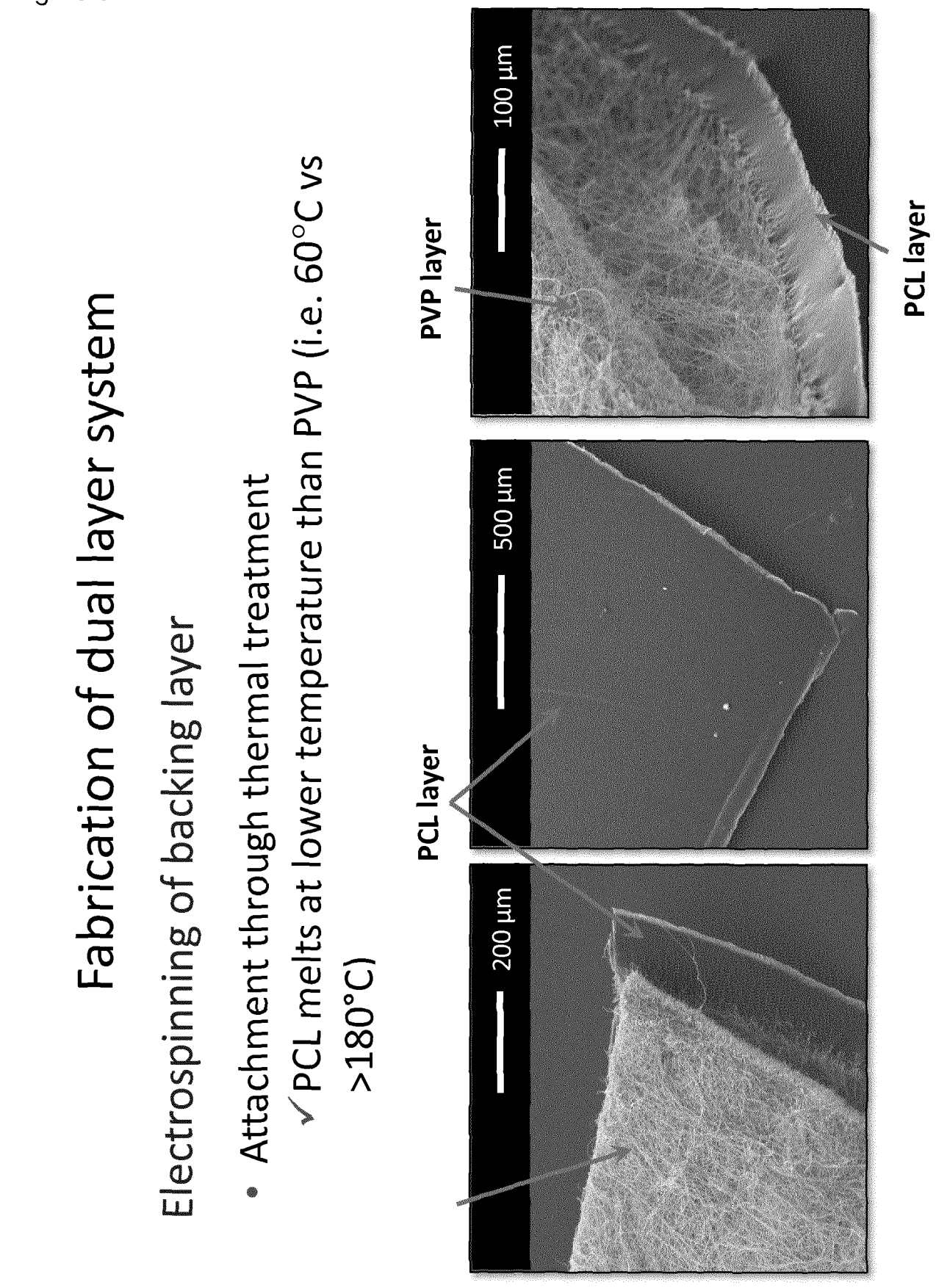

Fabrication of dual layer system
Electrospinning of backing layer
• Attachment through thermal treatment
✓ PCL melts at lower temperature than PVP (i.e. 60°C vs >180°C)
PCL layer
200 µm
500 µm
PVP layer
100 µm
PCL layer

Figure 10

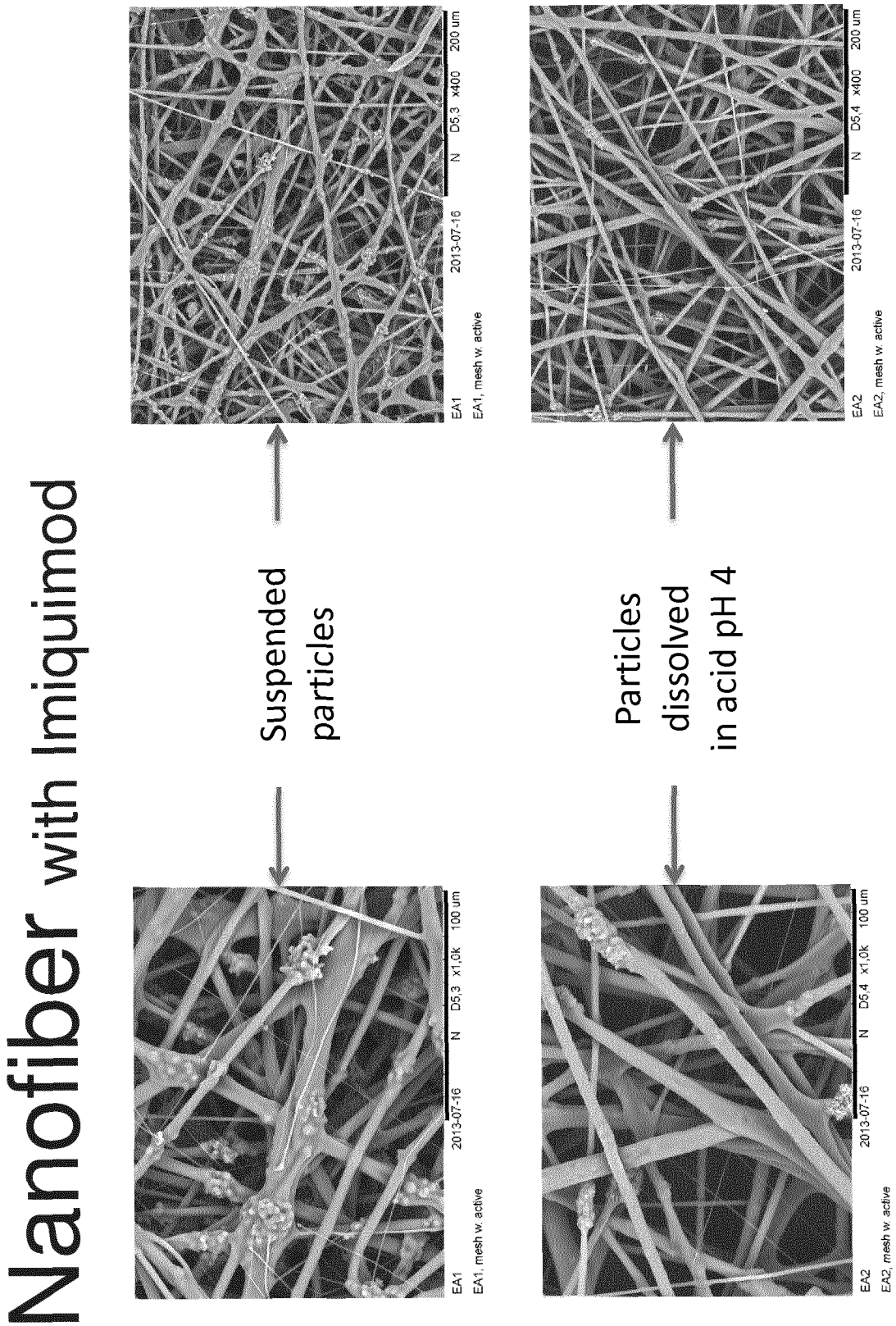

Nanofiber with Imiquimod
Suspended particles
Particles dissolved in acid pH 4
EA1
EA1, mesh w. active
2013-07-16
D5,3 x400 200 um
D5,3 x1,0k 100 um
EA2
EA2, mesh w. active
D5,4 x400 200 um
D5,4 x1,0k 100 um

Figure 11

Tensile Testing of Rivelin Patch
Bose Electroforce 3100
9mm original length between clamps
Displacement of 0.02mm/s to 6mm
Young's modulus – measure of stiffness
% elongation
Ultimate tensile strength
Stress
Strain
1
0,8
0,6
0,4
0,2
0
-0,2
0
0,1
0,2
0,3
0,4

Figure 12

Residence Time of Rivelin Patch on Porcine Oral Mucosa
Porcine mucosa adherence to petri dish using cyanoacrylate glue
Saliva aerosol onto surface of porcine mucosa
5 second applied force
Mucosa sub-merged in PBS (simulated saliva)
30-50rpm mechanical stirring
Residence time = time taken for patch detachment
Residence time (minutes)
0
10
20
30
40
50
0%
5%
10%
15%
30rpm
40rpm
50rpm

Figure 13

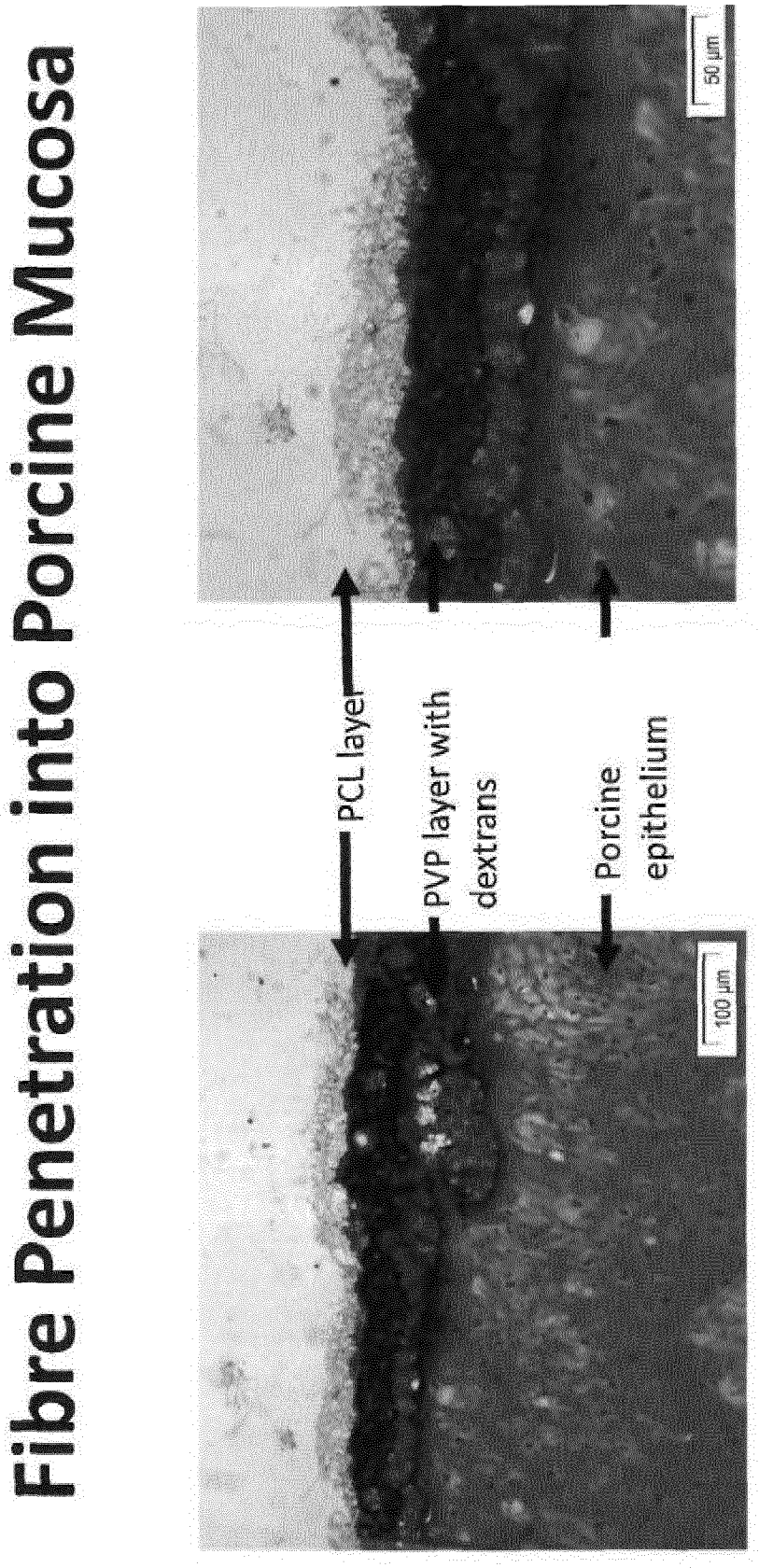
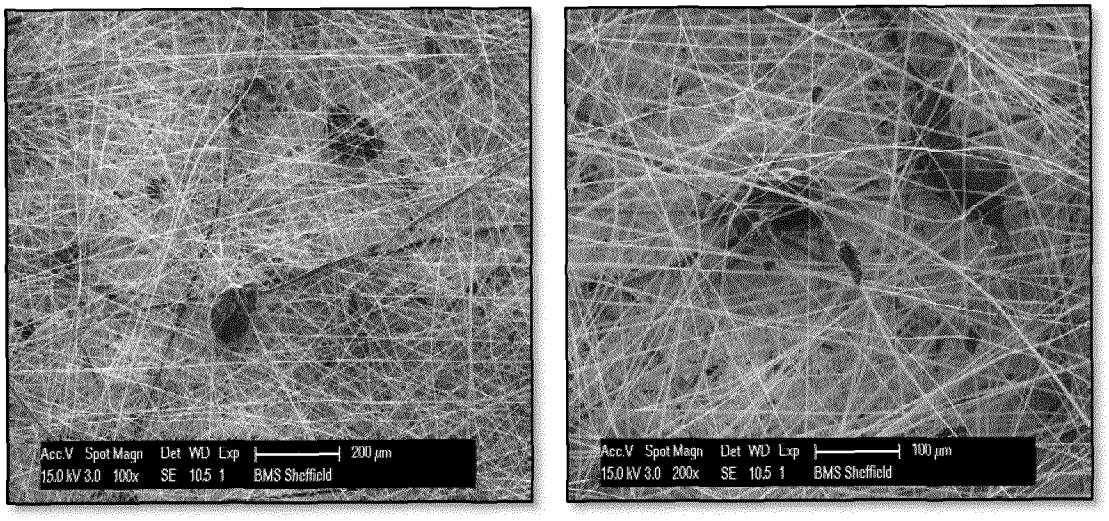

Fibre Penetration into Porcine Mucosa
PCL layer
PVP layer with dextrans
Porcine epithelium
50 µm
100 µm

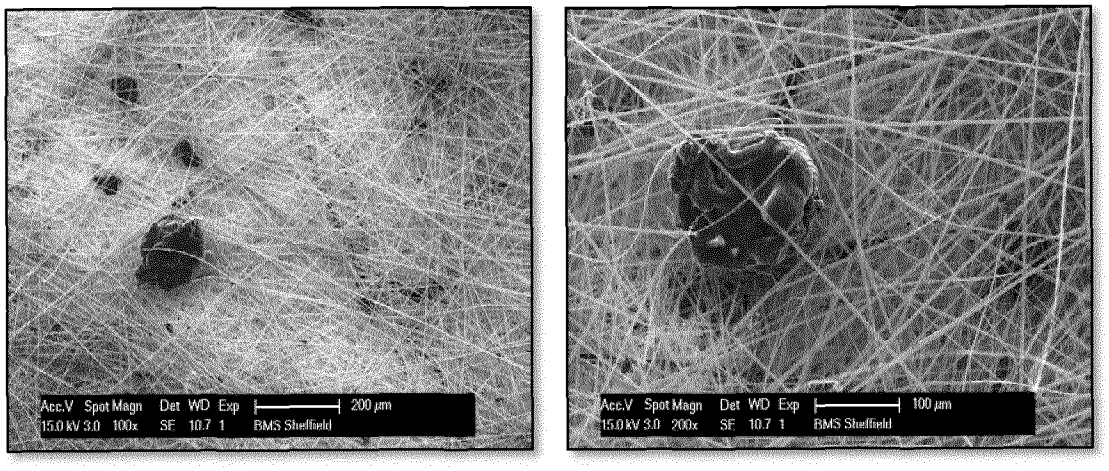
Figure 14

Eudragit L100-55 + Sodium alginate



A B

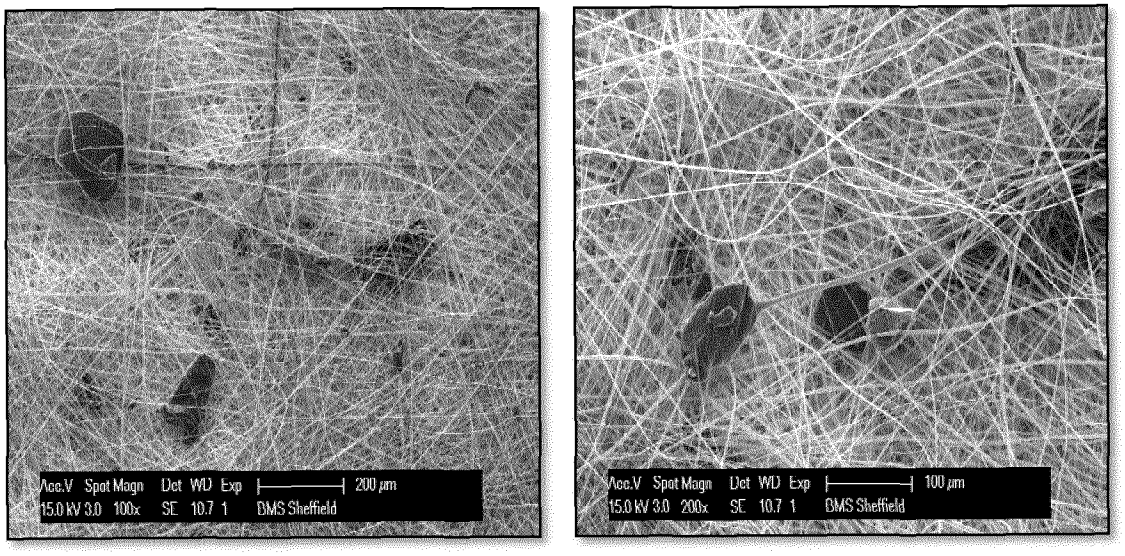
Eudragit L100-55 + Sodium carboxymethyl cellulose



C D

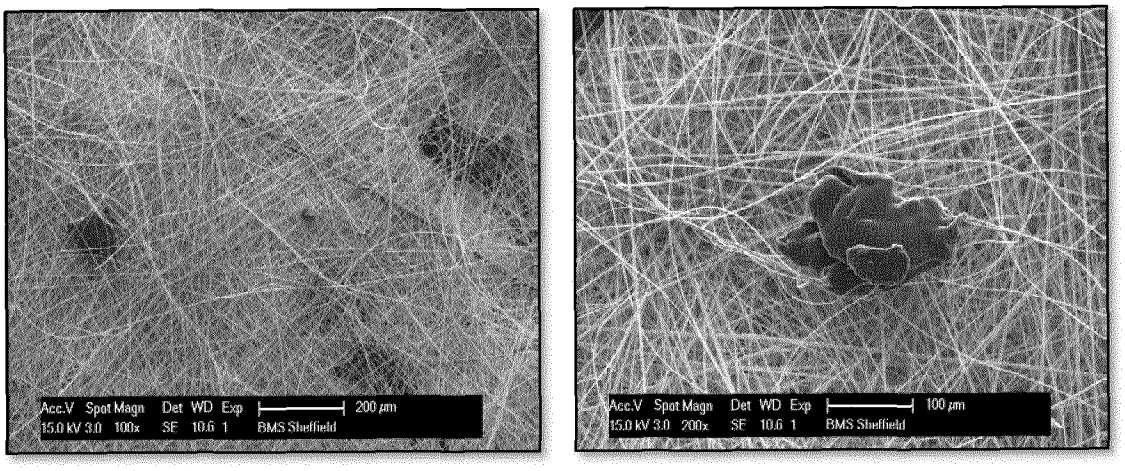
Figure 15

Eudragit L100-55 + Chitosan



A B

Eudragit L100-55 + Poly(vinyl alcohol)



C D

Figure 16



1) L100-55
2) L100-55 + Dextran
3) L100-55 + Polyethylene oxide
4) L100-55 + Carboxymethyl cellulose
5) L100-55 + Poly(vinyl alcohol)
6) L100-55 + Chitosan
7) L100-55 + Alginate