Medical용 섬유소재의 연구개발동향

헬스케어 섬유소재

2015

ECO융합섬유연구원

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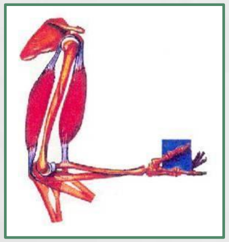
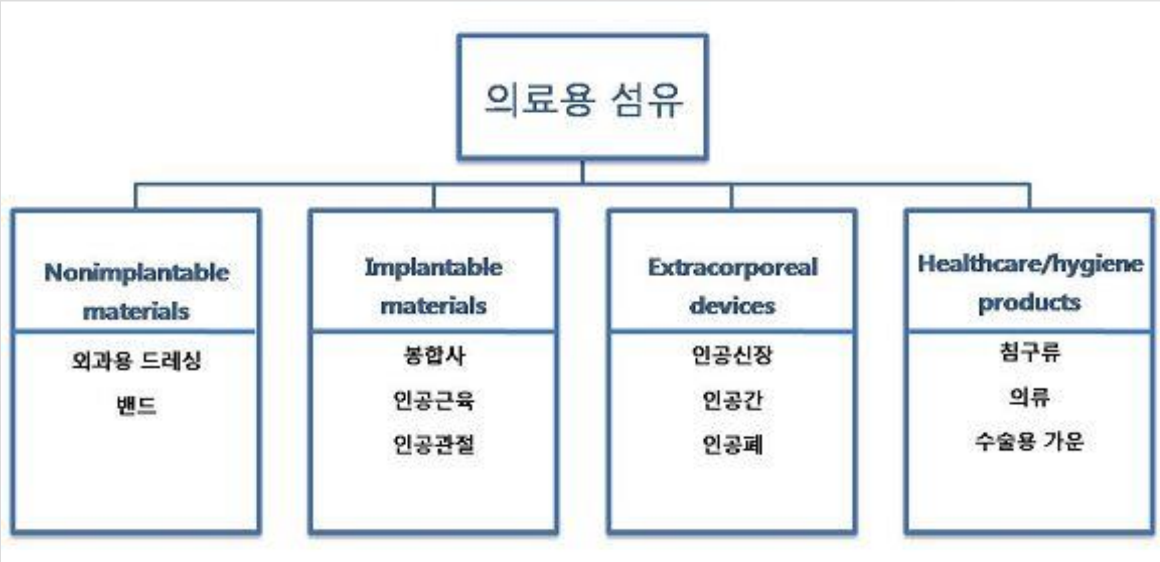


◎ Recent Research Achievements
& Potential Applications

Biomedical Textiles

의료용 소재



메디컬 기능을 갖는 소재
- 신체치료, 건강회복 등에 사용
- 헬스케어 기능을 갖는 섬유로서 신체활성, 건강증진에 사용
- 인체보호 기능을 갖는 소재

생체기능성

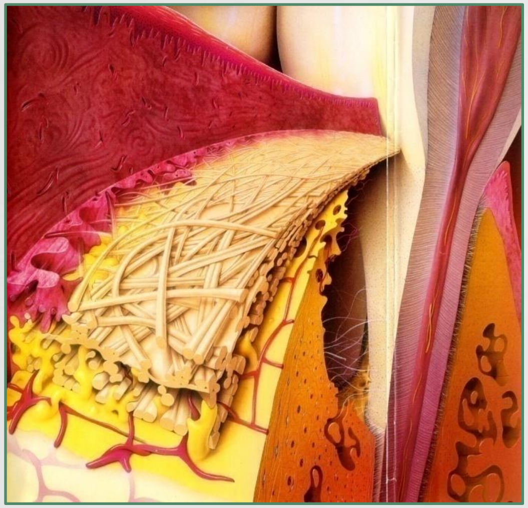
- 멸균성
- 성형가공성 및 형태 유지
- 기계적 물성 및 내구성
- 화학적 안정성
- 재현성

생체적합성

- 생체거부 반응이 없음
- 인체 내 구성성분(단백질 등) 흡착으로 인한 기능저하가 발생하지 않음

생체적합성재료 (BIOCOMPATIBLE MATERIALS)
- 혈액적합성 (Blood Compatibility)
- 조직적합성 (Tissue Compatibility)

의료용 소재: 부직포



생분해성 부직포로 제조된 Guided Tissue Regeneration (GTR) Barrier

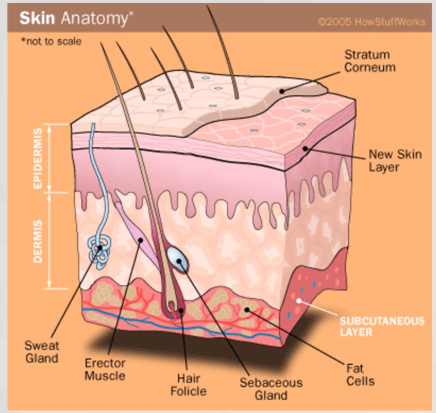
- 부직포의 특징

- 두께를 자유롭게 변형
- 다공성으로 통기, 흡수성, 보온성이 우수
- 사용되는 섬유와 binder가 합성고분자로 형태 안정성, 탄성이 양호
- 속건성으로 후처리가 불필요
- 열접착 가능
- 직물에 비해 인장강력은 작고 신도가 큼
- 생산성이 매우 우수

의료용 소재: 드레싱 소재

피부의 역할

- ▶유체나 전해질 평형 유지
- ▶유해균으로부터 신체의 보호
- ▶체온유지
- ▶감각
- ▶외형유지



피부의 구성

- ▶표피(epidermis)
- ▶진피(dermis)
- ▶피하 세포 및 지방 (subcutaneous tissue and fat)
- ▶ 근육(muscle)

상처의 치유과정

염증기(inflammation)

↓

육아기(granulation)

↓

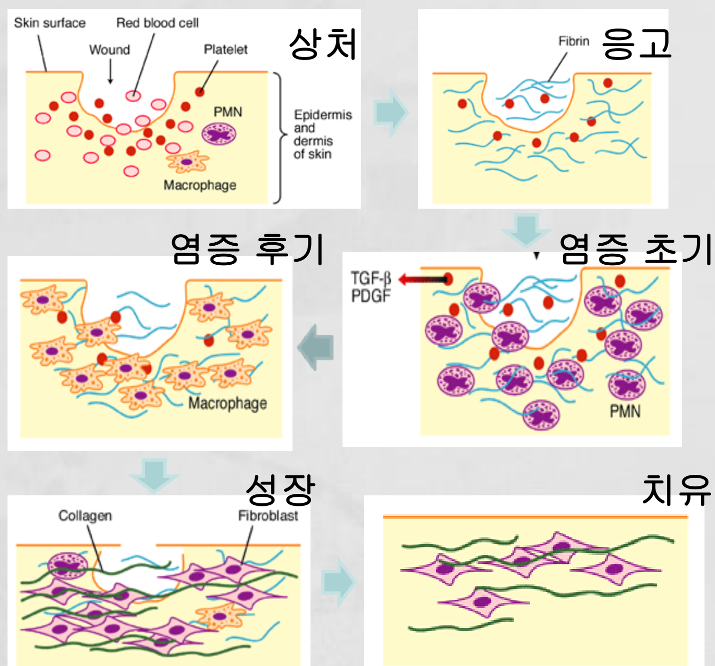
상피하기(epithelialization)

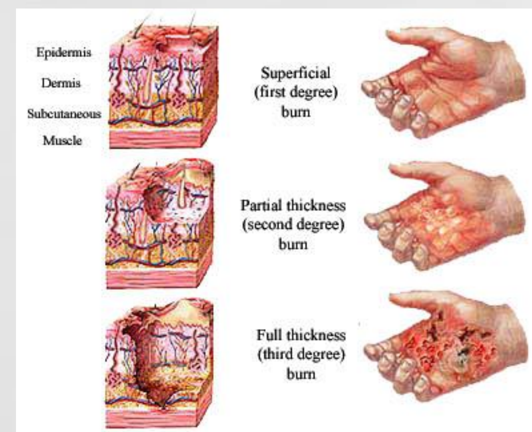
↓

섬유증식기(fibroplasia)

↓

수축기(contraction)





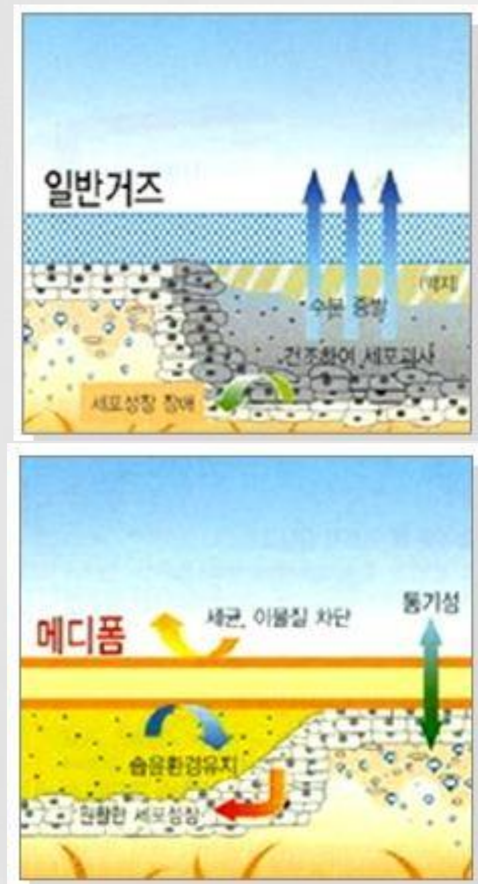
의료용 소재: 드레싱 소재

이상적인 Dressing의 요구조건

- ▶ Handling excess exudate
- ▶ Removal of toxic substances
- ▶ Maintenance of moist environment over wound
- ▶ Gaseous exchange permitted
- ▶ Barrier to microorganisms
- ▶ Thermal insulation provided
- ▶ Freedom from particulate contaminants demonstrated

메디폼

친수성 드레싱



의료용 소재: 드레싱 소재

창상피복재의 종류

Gauze : 상처표면을 덮고 제거될 때 상처를 붕괴시킴
적은 상처부위에 사용되며 주로 이차 드레싱용으로 사용됨

Tulle : 상처표면에 고정되지 않음. 평면의 얇은 상처에만 적용함
Jelonet ®, Paranet ®

Semipermeable film :
아크릴 접착제가 코팅된 PU 시트상임
상처 경과를 확인할 수 있도록 투명함
적은 삼출액을 가진 얕은 상처에 사용됨
OpSite ®, Tegaderm ®

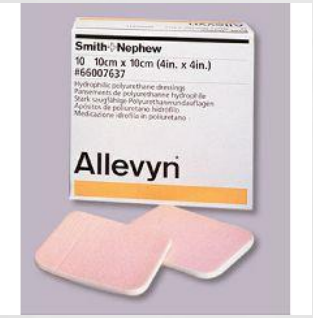
하이드로 콜로이드:
- 삼출액을 흡수할 경우에 겔로 변함
- Carboxymethylcellulose, gelatin, pectin elastomer와 접착제로 구성됨
- 삼출액의 양이 많거나 허물(sloughing) 또는 육아(granulating) 상처에 적용
- DuoDERM®, Tegasorb®

하이드로겔:
- 고분자 겔을 포함하는 섬유나 네트워크 복합체에 물이 함유된 형태임
- 상처의 습도를 유지하기 위하여 물이 방출됨
- 죽은 조직의 제거와 재수화(rehydrate)를 위하여 괴저 또는 허물 상처에 사용됨
- Tegagel®, Intrasite®

의료용 소재: 드레싱 소재

알지네이트 :
- 칼슘 알지네이트(해초의 성분)로 구성됨
- 상처에 붙이면 칼슘이 나트륨으로 바뀌면서 드레싱이 겔로 변하여 상처의 습윤상태를 유지함
- 삼출액이 많은 상처에 적합함
- Kaltostat®, Sorbsan®

폴리우레탄 또는 실리콘 폼:
- 많은 양의 삼출액을 흡수함
- 상처의 습윤상태를 유지하나 알지네이트나 하이드로 콜로이드 만큼 괴사에 유용하지 않음
- Allevyn®, Lyofoam®

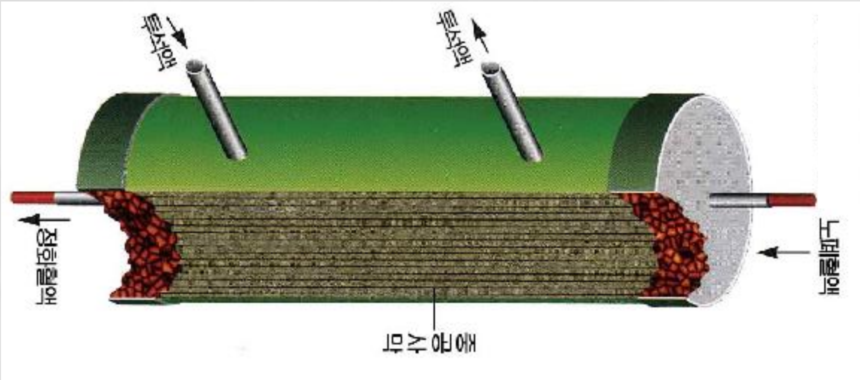


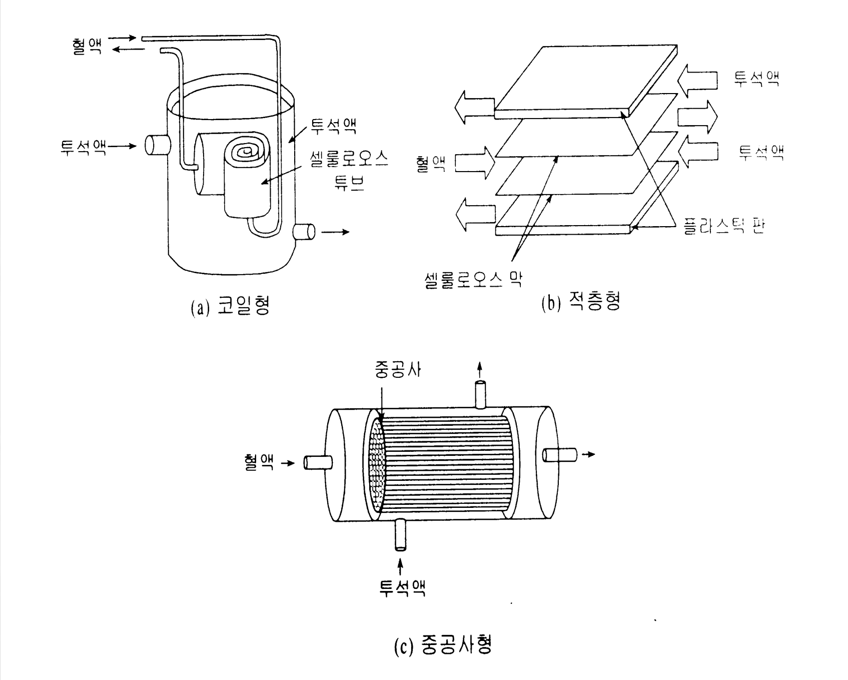
하이드로파이버 :
- Sodium carboxymethylcellulose 섬유로 만들어진 부드러운 부직포 패드 또는 리본 드레싱
- 부드러운 겔을 형성하기 위하여 상처 배액과 반응함
- 깊은 상처에 습윤환경과 삼출액을 흡수함

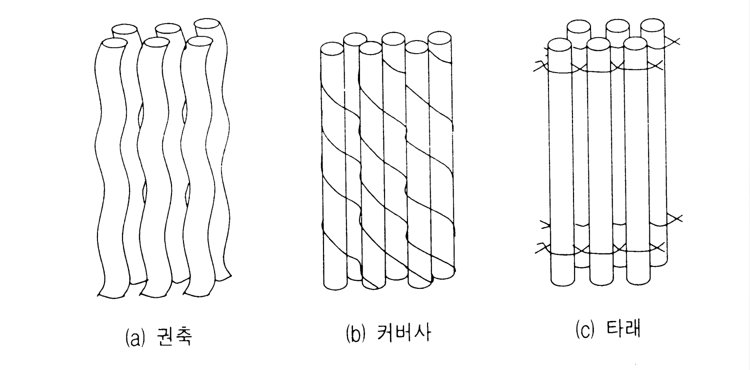
콜라겐 :
- 패드, 겔 또는 입자 형태가 있음
- 새로 형성된 콜라겐의 침전을 증진시킴
- 삼출액을 흡수하고 습윤환경을 제공함

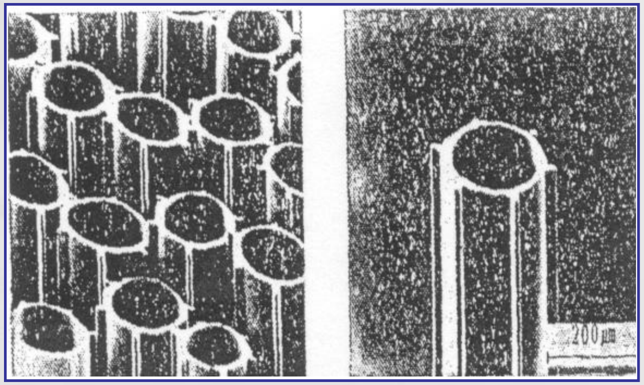
의료용 소재: 혈액정화용 소재

- 혈액 중 대사물질인 노폐물(요소, 요산, 크레아틴 등)의 제거에 사용되며 다수의 중공사(직경 200~300㎛)로 혈액 투석막은 현재 cellulose가 주류를 이루고 있다.





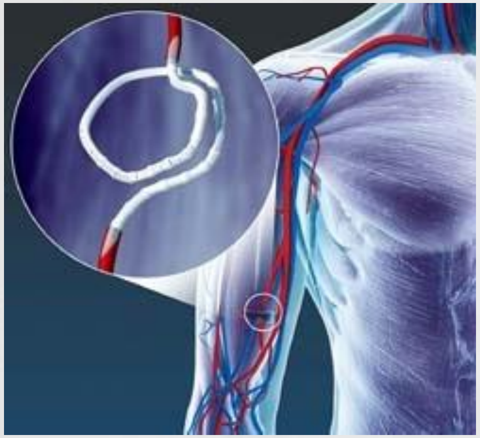




6개의 돌기가 있는 중공사

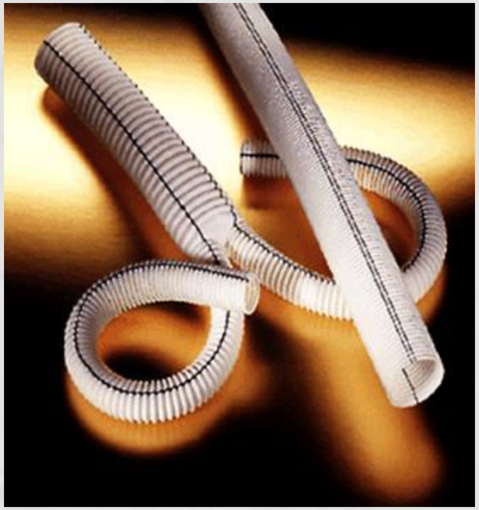
의료용 소재: 인공혈관용 소재

- 우수한 항응혈성과 적절한 기계적 강도가 요구되고 합성에 의한 것과 생체에 의한 것으로 나눌 수 있으며 아직 모두 완벽한 형태는 아니다. 다공성의 PET 및 PTFE 가 사용된다.
(대구경 인공혈관)

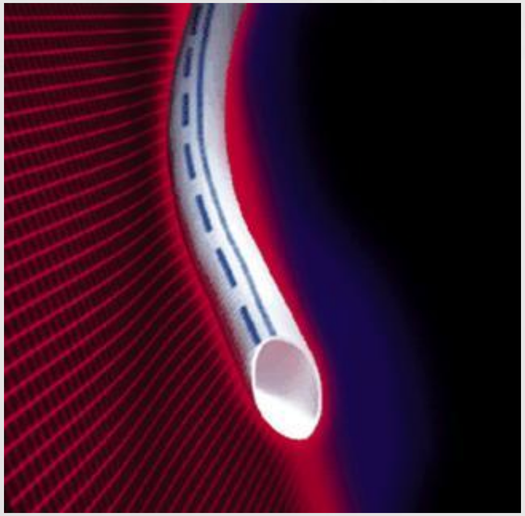


<현재 사용중인 제품>

SEAL Bifurcated Stent Graft



Hemashield Gold™ Textile Vascular Grafts



Meadox Exxcel™ ePTFE Vascular Grafts

의료용 소재: Scaffold 소재

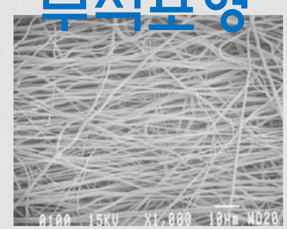
다공성 스캐폴드의 재료 및 가공법

재료	가공법	응용
Poly(α-hydroxy ester) Poly(L-lactide)(PLLA)	SCPL, PS, RP, woven, FD, MM, Extrusion, ML	Bone, Liver, Cartilage, Nerve
Poly(glycolic acid)(PGA)	Nonwoven	Bone, Cartilage, Liver
PLLA/PGA	FB	Bone, Cartilage, Liver
Poly(D,L-lactic-co-glycolic acid)(PLGA)	SCPL, GF, RP, Extrusion, ML, FD, MM	Bone, Liver, Cartilage, Nerve Urothelium, Blood vessel
Poly(L-lactic-co-ε-caprolactone)(PLLACL)	Extrusion, ES	Blood vessel, Nerve, Meniscal tissue
Poly(D,L-lactic-co-ε-caprolactone)(PLACL)	PS, SCPL	Blood vessel
Polyhydroxy alkanoate(PHA)	PS	Blood vessel
Poly(ε-caprolactone)(PCL)	ES	
Poly(propyrene fumarate)(PPF)	ES	Bone
Polydioxane	SCPL, FD	Cartilage, Bone

스펀지형

직물형

부직포형



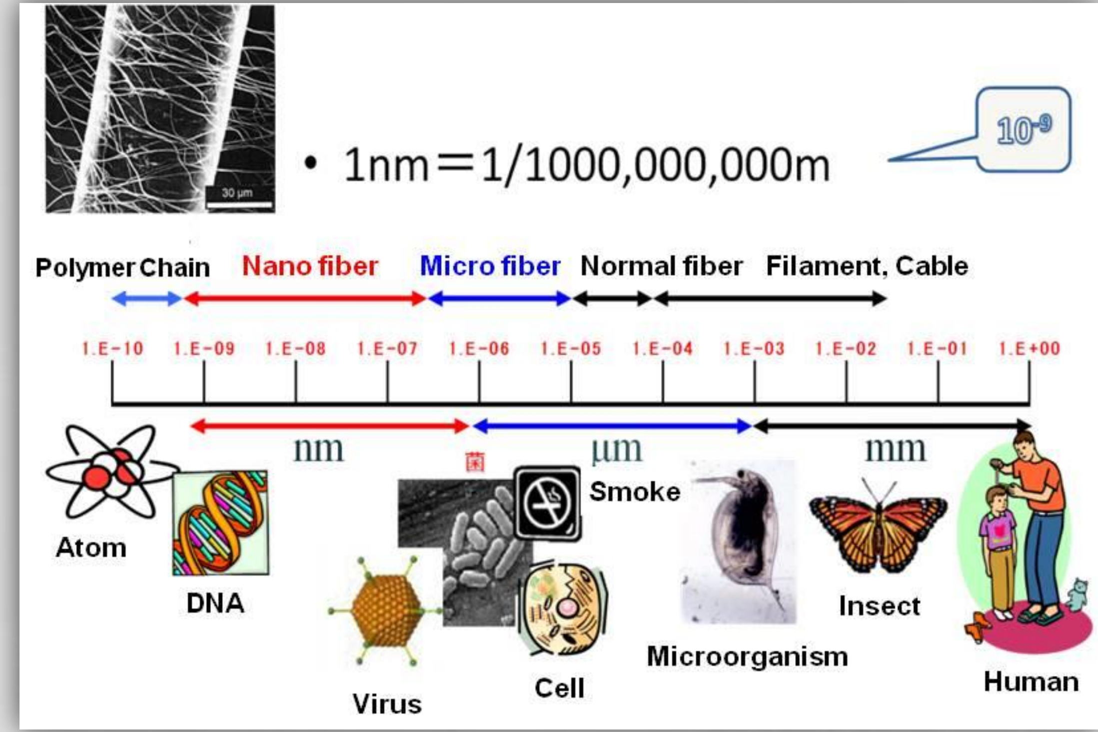
소프트 일렉트로닉스

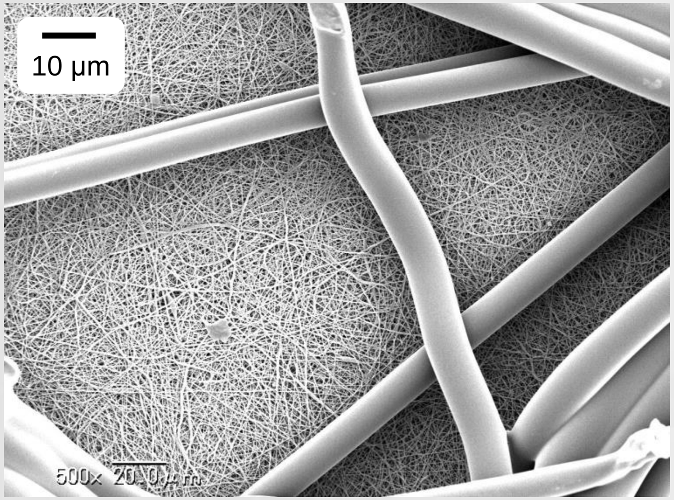

생체친화형 전자소자
Electronic contact lens
자가진단 바이오칩
형태변형 단말기
Solar backpack
E-Skin
Wearable electronics
플렉서블 전자종이

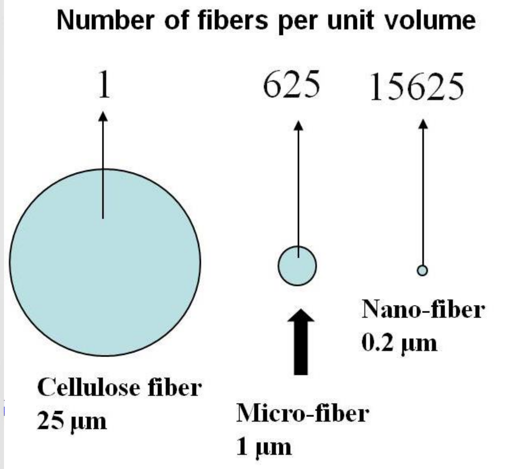
소프트 플랫폼 기술
소프트 소자 기술
Light-emission
Light-emitting Semiconductor
Source
Gate
Drain
소프트 나노소재 기술
Graphene
P-type
N-type
Core-shell fiber (P3HT, PCBM)
소프트 나노공정 기술
Mirco fiber
Roll up fiber
Microwire
Drawing fiber
소프트 나노소재 / 나노공정 / 나노소자 / 플랫폼 기술
융합
나노기반 고성능 소프트 일렉트로닉스

Introduction: Why Nanofiber?

Introduction: Why Nanofiber?





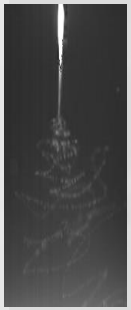


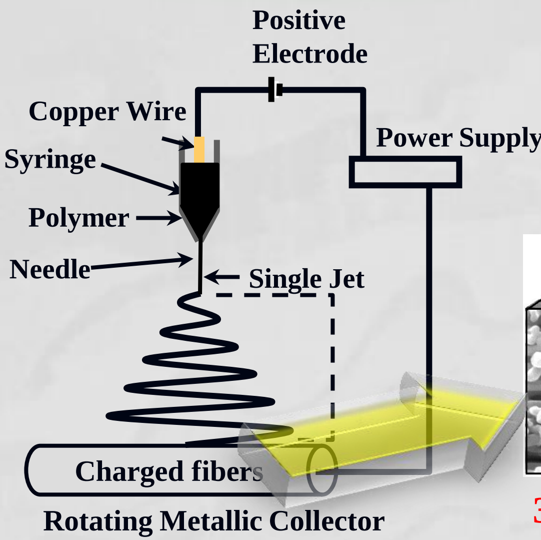
Small but Great Effect !

from Phillip Gibson and Heidi Schreuder-Gibson, U.S. Army Soldier Systems Center, Natick

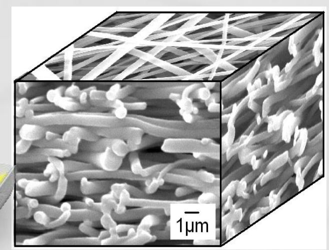
Electrospun Nanofibers: Electrostatic Spinning

Nanofiber ···



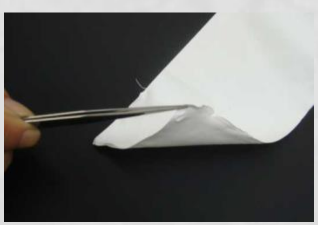


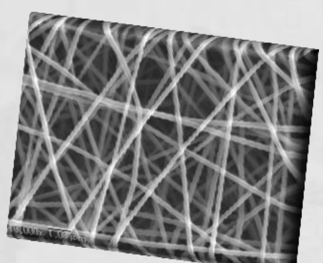
Schematic of electrospinning



3D structure of E-spun fibers

One of top-down manufacturing processes to produce polymer fibers





Electrospinning

History

1902	Initiative
1934	Patenting **(By Formhals)**
Early 1990s	Activation **(By Reneker)**

Characteristics of electrospinning;

- **Various polymers are available**
- **Low cost for production**
- **Controlled diameter of the fibers from nano- to micrometers**
- **Easy processing**
- **Direction preparation of fabric sheets**

System parameters

- **Mw &MWD, architecture(branched, linear etc.) of the polymer**
- **Solution properties (viscosity, conductivity, and surface tension)**

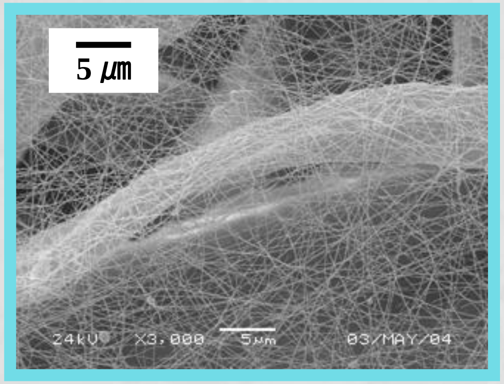
Processing parameters

- **Applied voltage, flow rate, concentration, distance between the capillary tip and collector, ambient parameters (temperature, humidity, air velocity in the chamber)**
- **Motion of collector**

Organic Polymers for Electrospinning

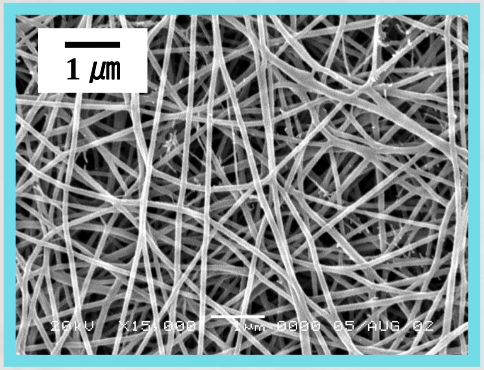
Nylon6, Nylon66, PVC, PU, PVC/PU, PVA, PVAc, PAN, PEI, PC, PSF, etc.

Coating



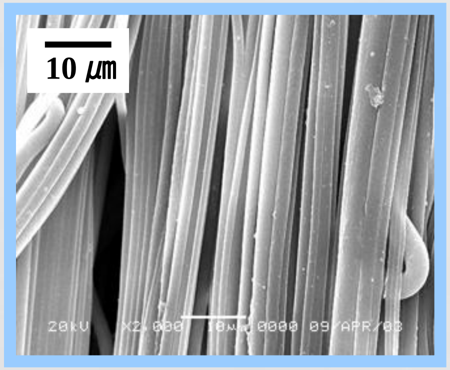
Nylon6, Nylon66, PU, PVA, PVAc, PAN, PEI, etc.
-Biodegradable polymers :PCL, PLA, PLGA, etc.

Nonwoven



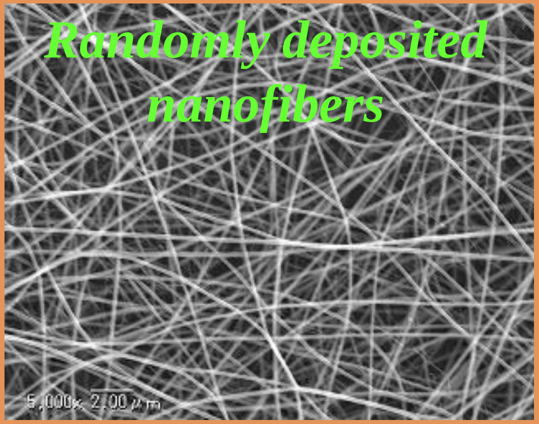
PU, PU/PVC, PCL Nylon6, Nylon66, PSF, etc.

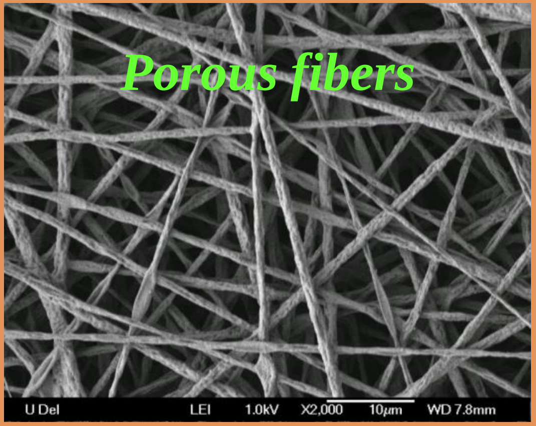
Filaments

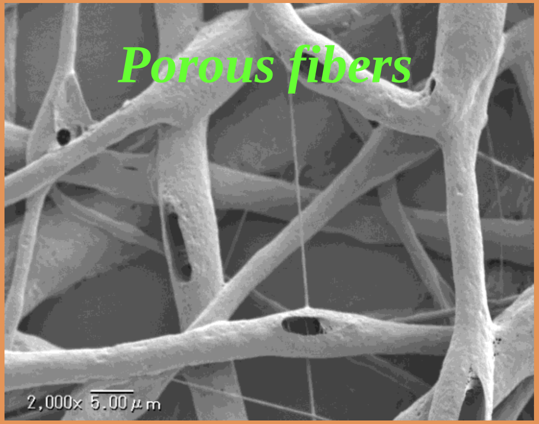


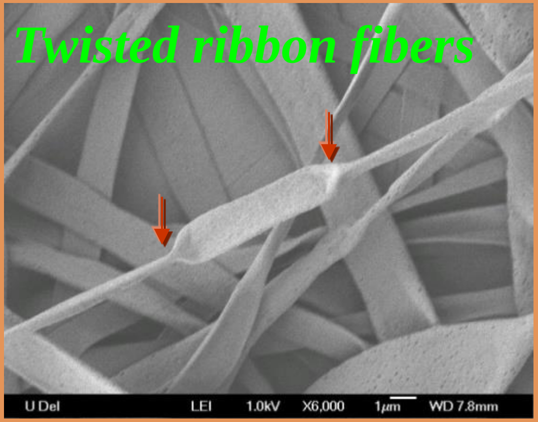
Key Technologies

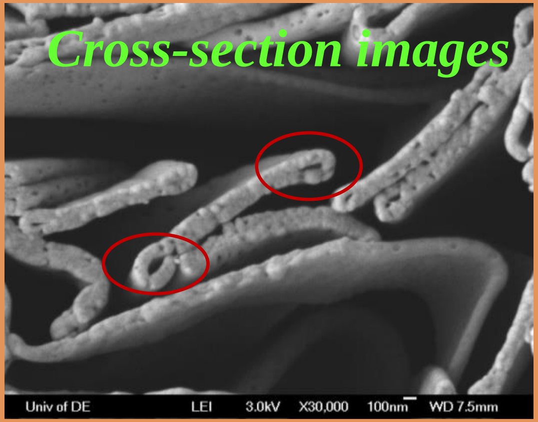
Various Nanostructured Electrospun Nanofibers





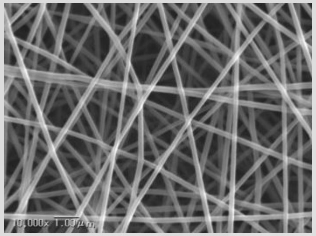




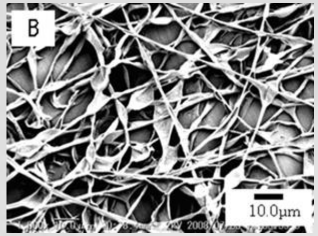


Various Electrospun Nanofibers

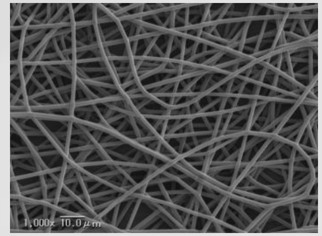
PVA



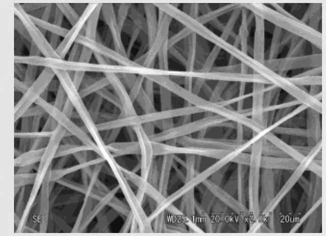
Poly(1-butene)



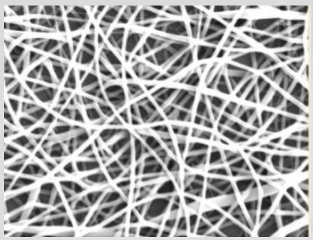
Polyvinyl acetate (PVAc)



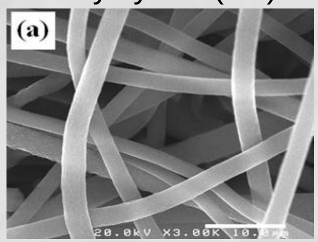
Poly-L-lactic acid (PLLA)



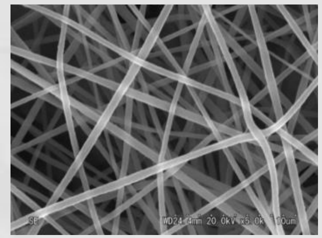
PP



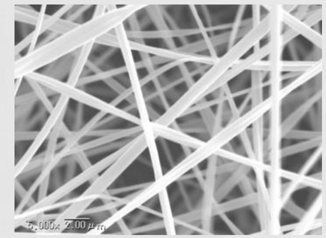
Polystyrene(PS)



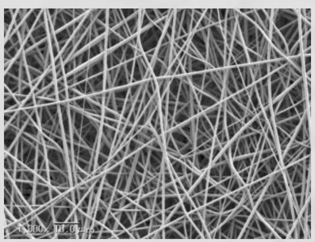
Poly(vinylidene fluoride)(PVDF)



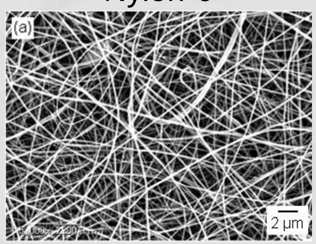
Cellulose acetate



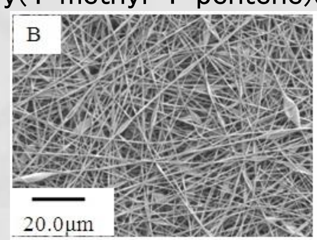
PVP



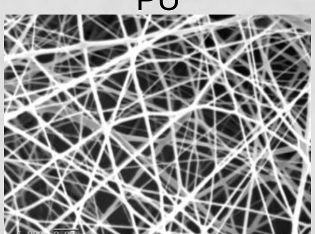
Nylon-6



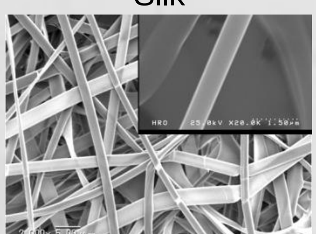
Poly(4-methyl-1-pentene)(PMP)



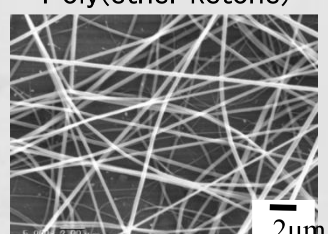
PU



Silk

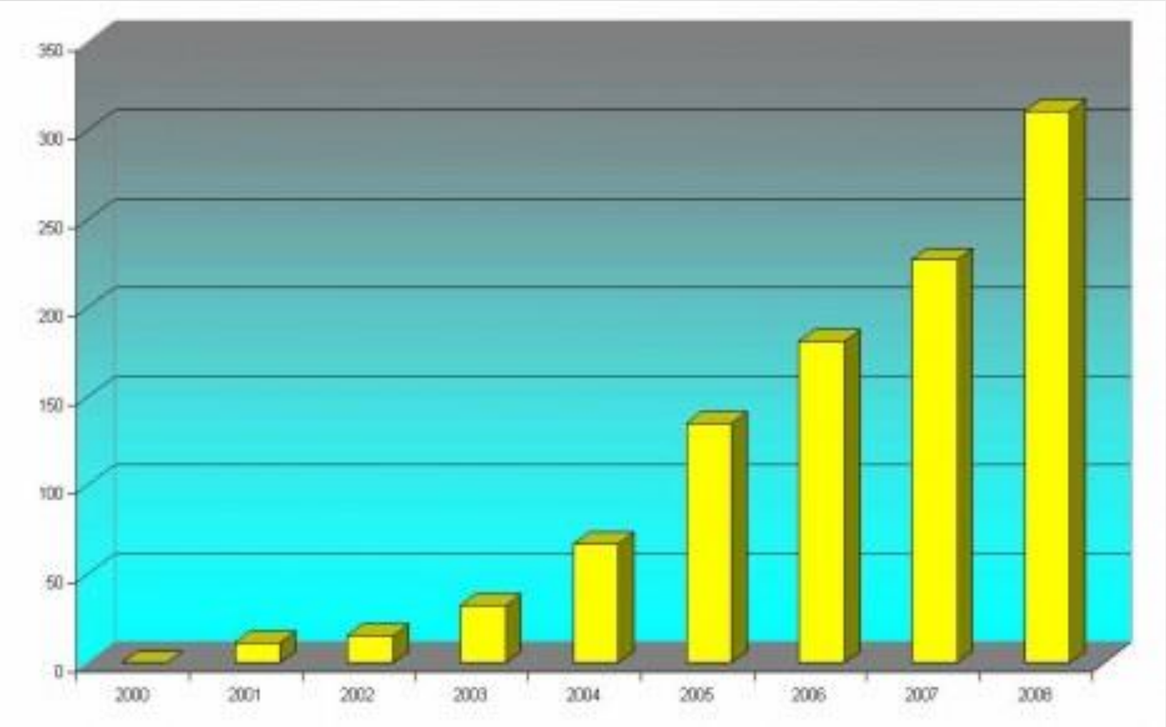


Poly(ether ketone)



Nylon66, PVC, PAN, PES, PCL, PLA etc.

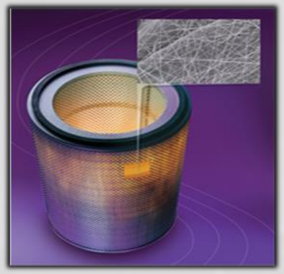
Nanofibers: volumetry in biomedical publications since 2000



This chart was built by searching PubMed for publications mentionning *nanofiber* or *nanofibers* in their title or abstract.

Potential Applications
& Recent Research Achievements

Various Potential Applications




Air filter

Liquid filter

Battery separator

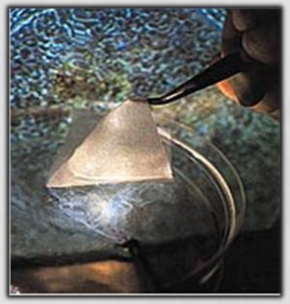
Advantages

- Large specific surface area
- Low air resistance
- Small pore size
- Lightweight

Disadvantages

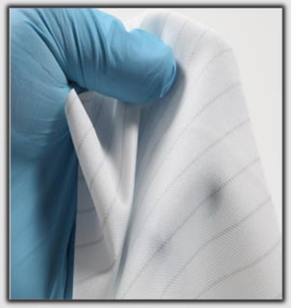
- Low mechanical properties
- Difficulty of mass production
- Risks on human health
- Environmental pollution

Outdoor wear



Medical uses


Carbon Fiber



Clean-room wiper

Recent Research Achievements

Healthcare

Biomedical
- **Nanofibrous scaffolds**
- **Wound dressing**
- **Drug delivery carriers**
- **Hydrogel nanofibers**

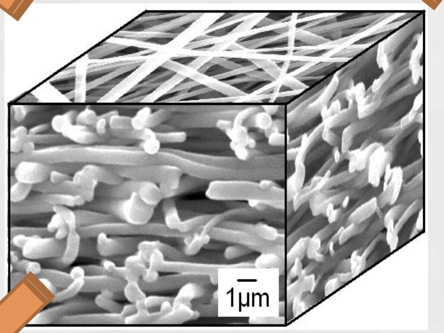
Nanofiber Assembly

Nanofiber filaments
- **High strength nanofiber filaments**
- **Shape memory nanofiber filaments**

Nanofiber tubes

Nanofiber capsules

Nanofibers



Energy

Electrics/Electronics
- **Metal nanofibers**
  - **Catalysts**
  - **EMI shielding materials**
- **Filters**
- **Separators**
- **Electrodes**

Nano-Characterization

Tensile test of single nanofibers
Friction test

J.C.Park, T.Ito, K.O.Kim, K.W.Kim, B.S.Kim, M.S.Khil, H.Y.Kim, I.S.Kim, *Polym. J.* **2010**, *42*, 273-276.
B. S. Kim, I. S. Kim, *Polymer Reviews* **2011**, *51*, 235-238.
K.Wei, Y.Li, K.O.Kim, Y.Nakagawa, B.S.Kim, K.Abe, G.Q.Chen, I.S.Kim, *J. Biomed. Mater. Res. A,* **2011**, *97A*, 272-280.
Y. Lee, J. Lee, D. Kimura, B. S. Kim, J. S. Koh, I. S. Kim, *Polym. Int.*, **2011**, *60*, 1442-1445.

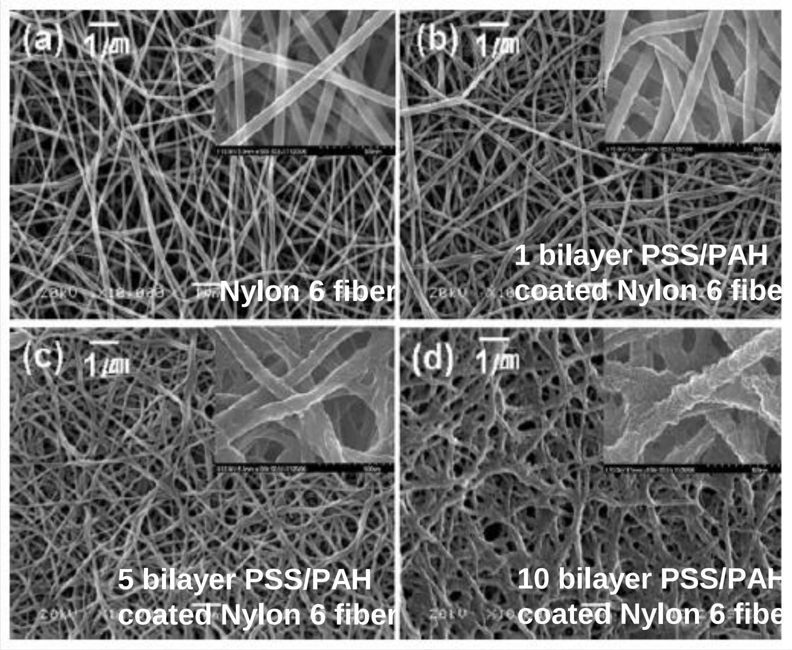
Nanocoating of Nanofibers via a Layer-by-Layer Self-Assembly Technique

Surface nanocoating

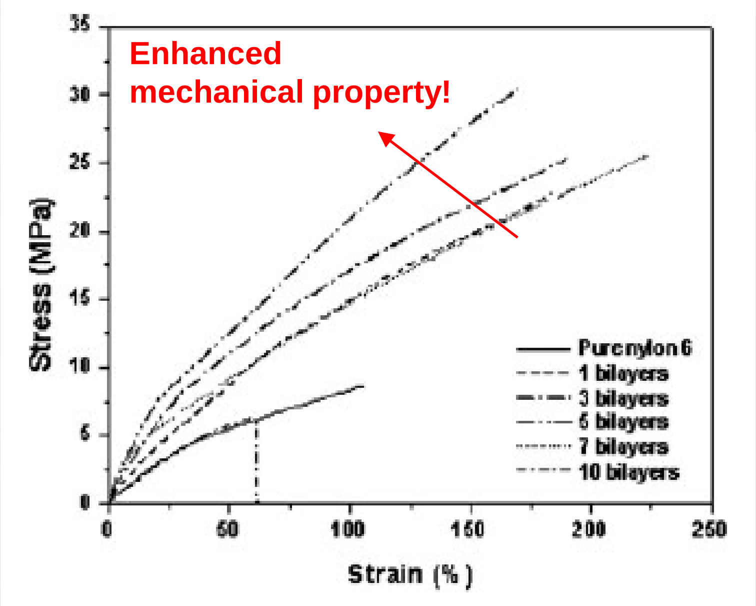
√ **Surface modification, such as *nanostructure and composition of the surface on the nanometer scale*, of the membranes or nanofiber mats by using a Layer-by-Layer self-assembly technique**

- Surface morphology, wettability, permeability, mechanics, cell growth, etc.

It may depend on the materials used, the nanostructured surfaces, and the thickness of the coated layer, etc.



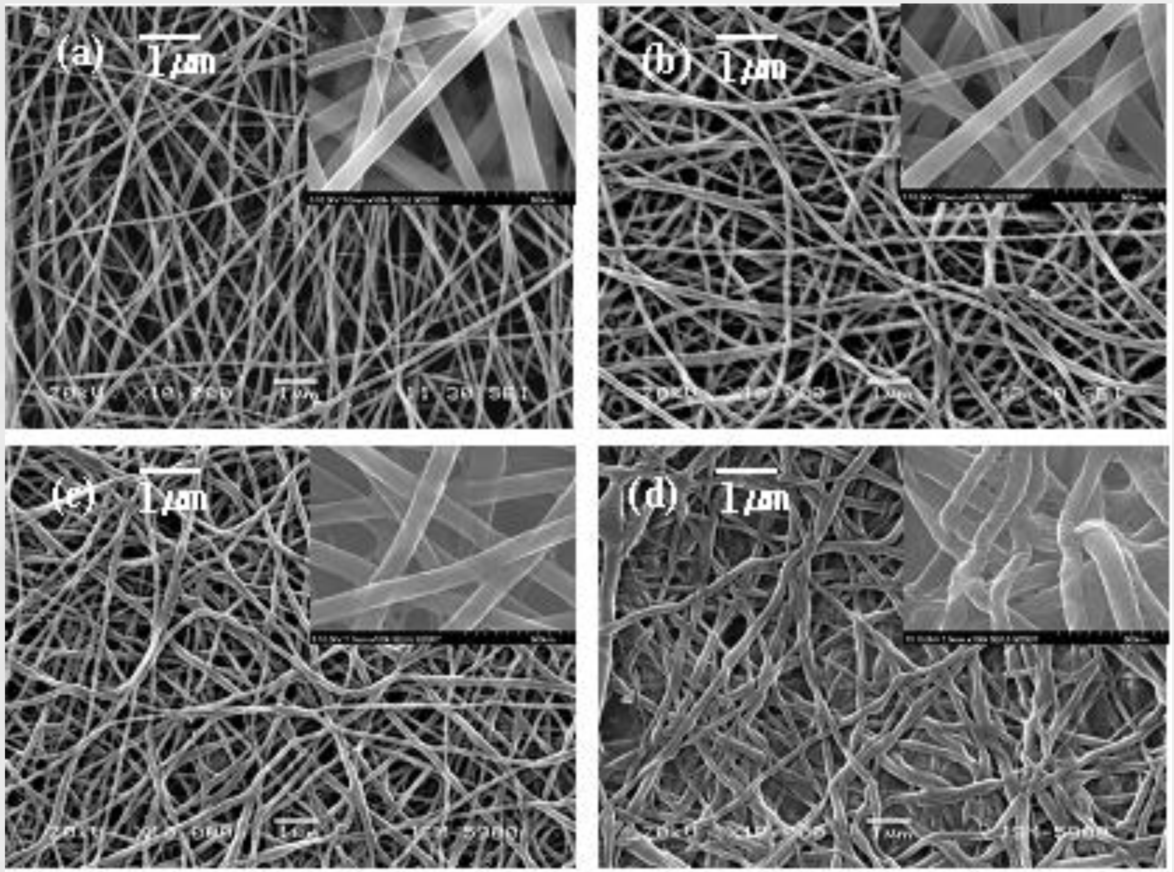
SEM images of surface nano-coated Nylon 6 fiber webs



Stress-strain curves of surface nano-coated Nylon 6 nanofiber webs

H. Y. Kim, J. H. Park, B. S. Kim, M. S. Khil, K. W. Kim, *Korean Patent 10-074090 8*, **2007**.
J. H. Park, B. S. Kim, M. S. Khil, H. Y. Kim, *J. Appl. Polym. Sci.* **2008**, *107*, 2211.

Nanocoating of Nanofibers via a Layer-by-Layer Self-Assembly Technique



SEM images of (a) electrospun nylon 6 fibers and polyelectrolyte multilayer-coated nylon 6 fibers with different number of bilayer of chitosan and alginic acid sodium salt; (b) 1 bilayer, (c) 5 bilayers, and (d) 10 bilayers.

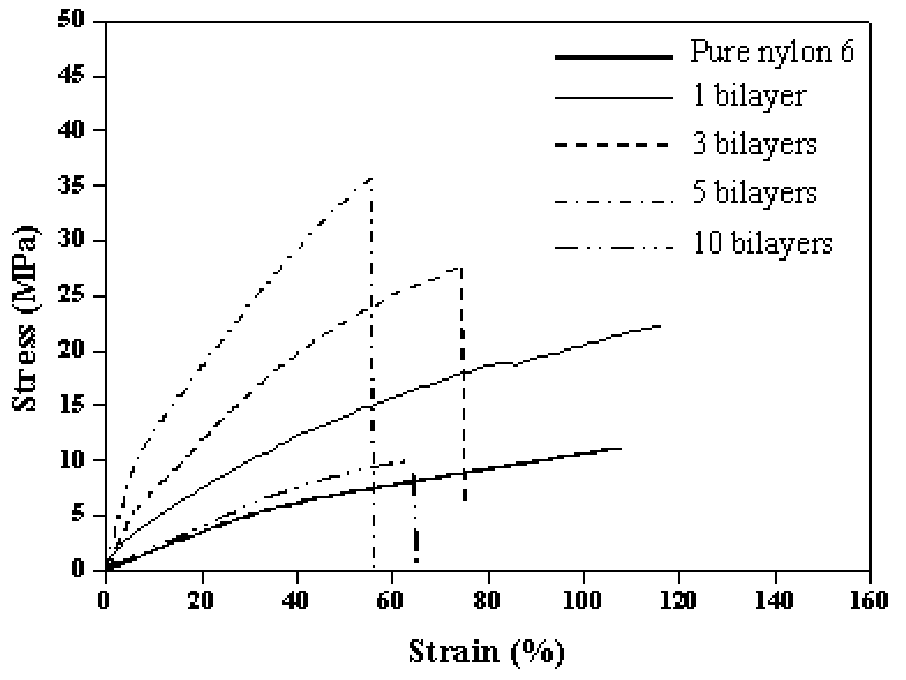


Figure 13. Stress-strain curves of pure nylon 6 fiber mats and polyelectrolyte multilayer-coated nylon 6 fiber mats with different number of bilayer of chitosan and alginic acid sodium salt

Bilayer number	Tensile Strength (MPa)	Young`s Modulus (MPa)	Elongation at break (%)
Pure nylon 6	10.6(±1)	16(±1)	115.3(±10)
1	22.9(±1)	57.2(±2)	123.7(±5)
3	29.3(±2)	124.3(±3)	77(±3)
5	35.2 (±2)	184.7(±3)	54.4(±10)
10	8.5(±1)	33.9(±1)	68.5(±15)

Table 3. Mechanical properties of pure nylon 6 fiber mats and polyelectrolyte multilayer-coated nylon 6 fiber mats

Nanocoating of Nanofibers via a Layer-by-Layer Self-Assembly Technique

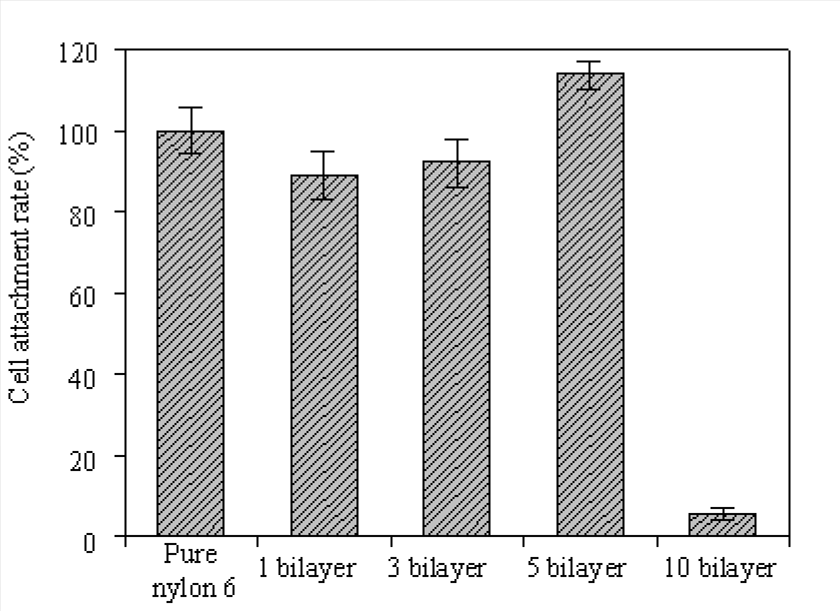


Figure 16. Attachment rate of chondrocyte in the cell-free area (mm2) of mats with different number of bilayers

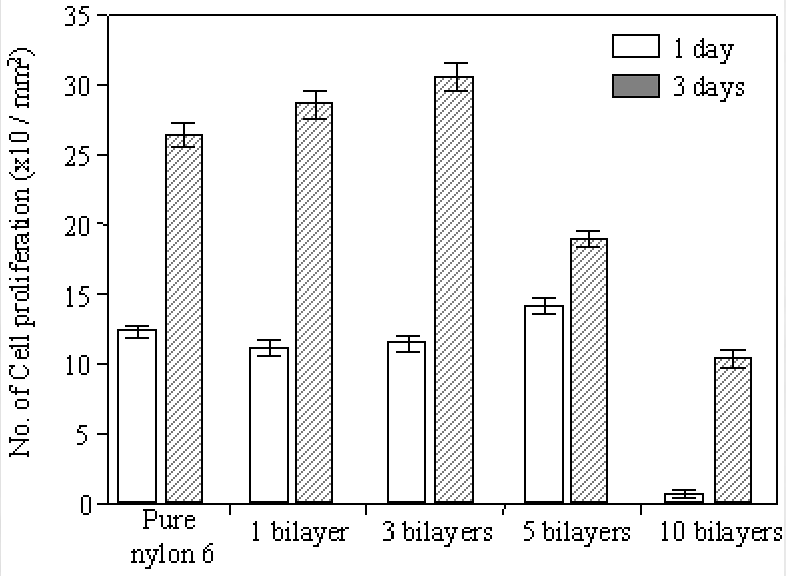
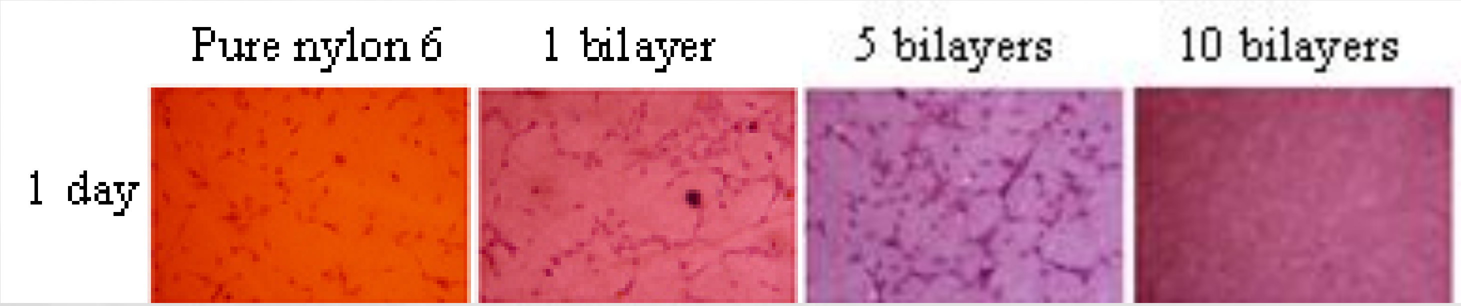
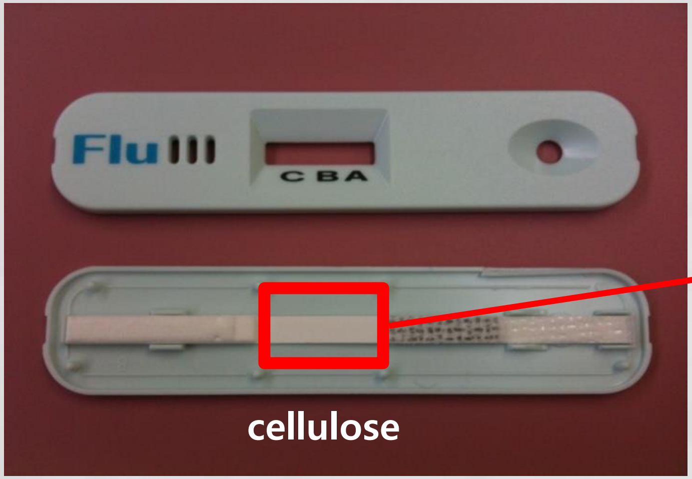
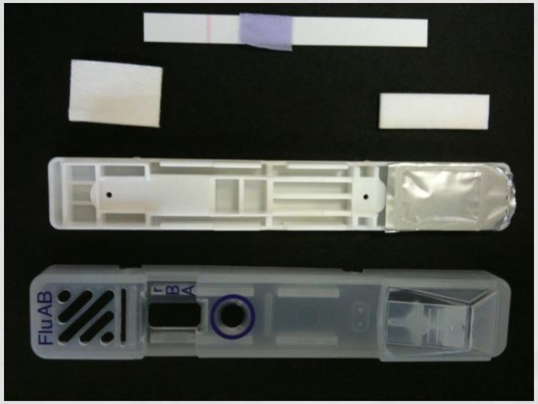


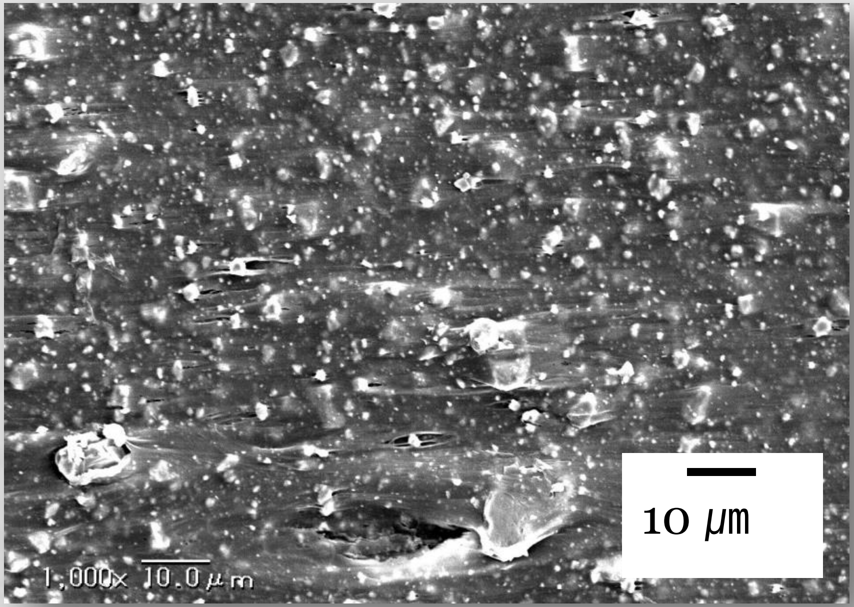
Figure 15. Cell proliferation of chondrocyte cultured on the mats with different number of bilayers for 1 and 3 days



Blood Sugar Bio-sensor







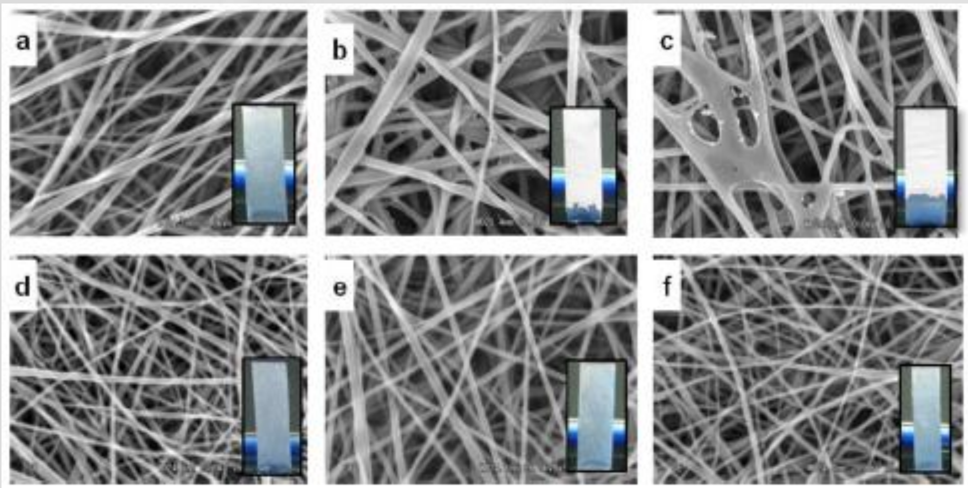
Expected blood sugar Bio-sensor

Using Nano-fibers

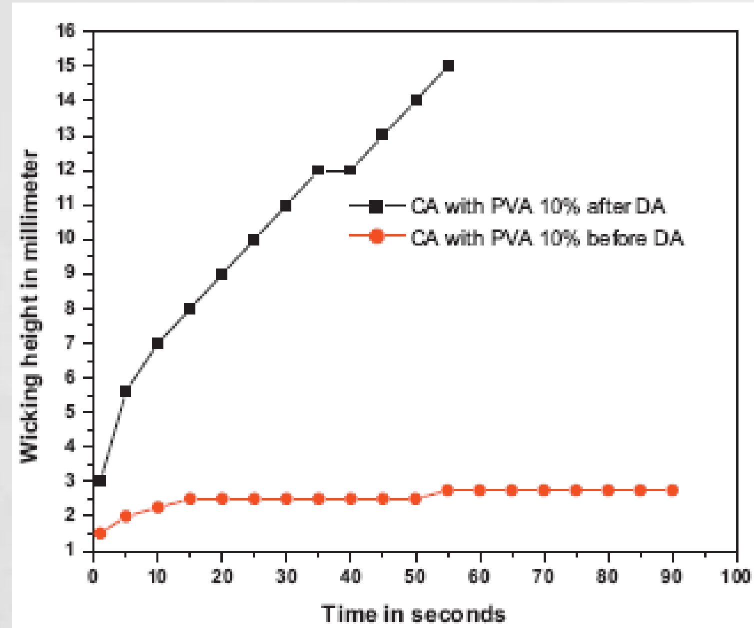
- **Very high sensitive**
- **Faster**

Wicking behavior of electrospun cellulose acetate nanofiber mats

SEM images taken after wicking ceased.
(a-c) before (d-f) after deacetylation.



Wicking rate



Water contact angle (°) before and after deacetylation.

Before deacetylation		After deacetylation	
CA	111.8°	CA	04°
CA/PVA (10%)	13.6°	CA/PVA (10%)	11.3°
CA/PVA (15%)	7.9°	CA/PVA (15%)	6.7°

Z. Khatri, K. Wei, B. S. Kim, I. S. Kim, *Carbohydrate Polymers*, in press.

Biomedical Application: 신경유도관

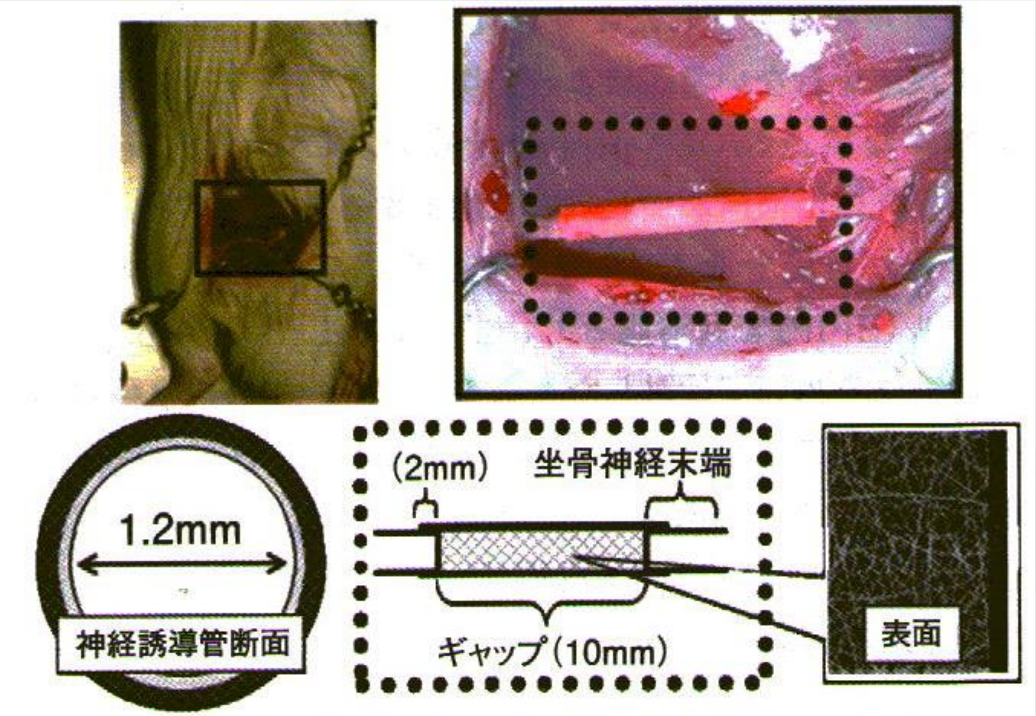
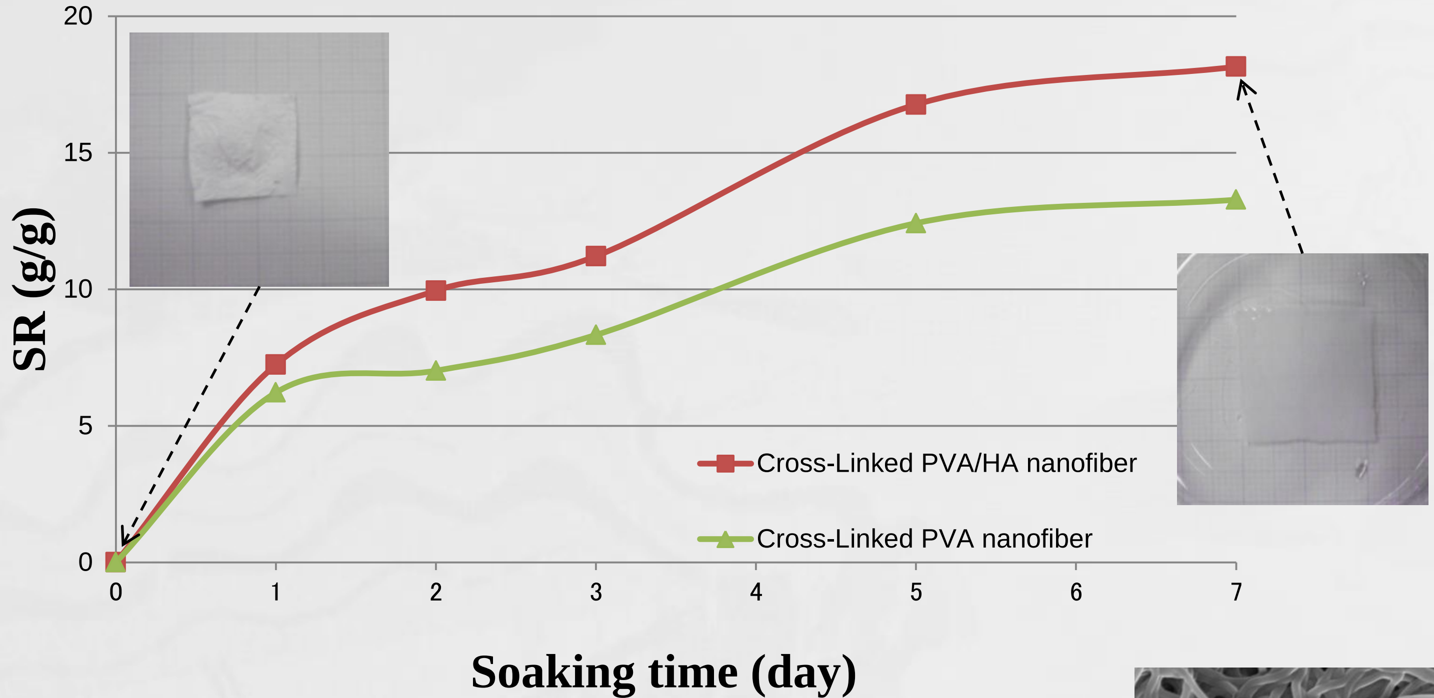


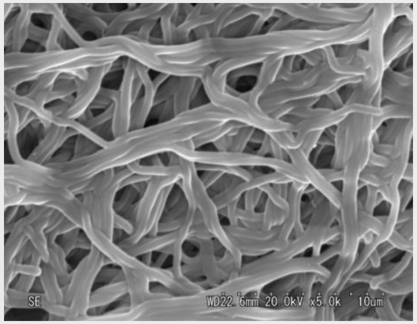
図 3　神経再生性機能ペプチド(IKVAV)で修飾されたナノファイバー神経誘導管

神経誘導管としての人工材料：ポリエチレンやシリコン

ナノ繊維からなる神経誘導管：
外界との物質交換が可能な多孔質材料でありながら、
周囲細胞の内空への浸潤を防御する多孔構造、さらに機能性付与も可能

Swelling Ratio of Hydrogel Nanofibrous Membranes



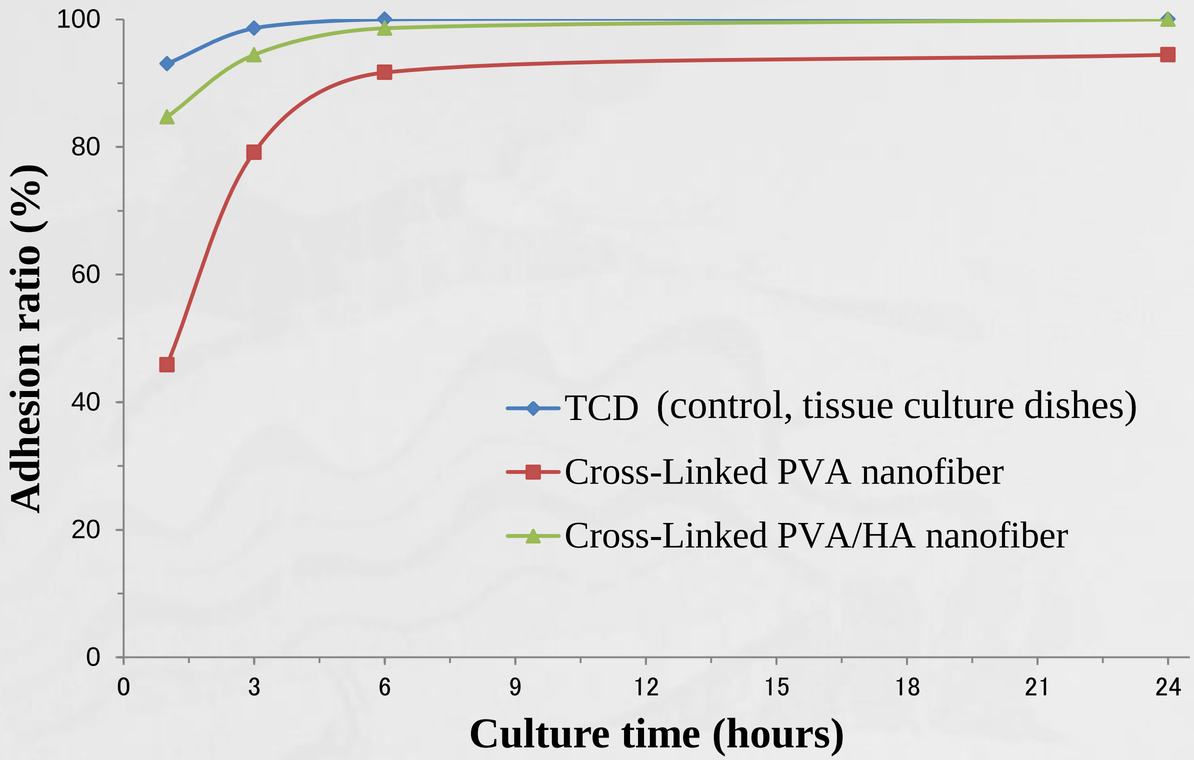


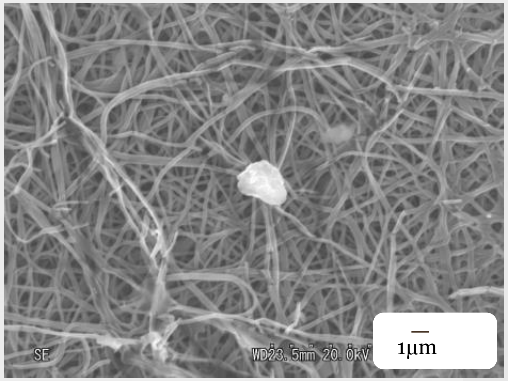
$$\text{Swelling Ratio (g/g)} = \frac{M_w - M_d}{M_d}$$

M_w : Mass of swollen nanofiber membrane

M_d : Mass of dried nanofiber membrane

Cell Affinity





$$\text{Adhesion Ratio (\%)} = \frac{C_s - C_f}{C_s} \times 100$$

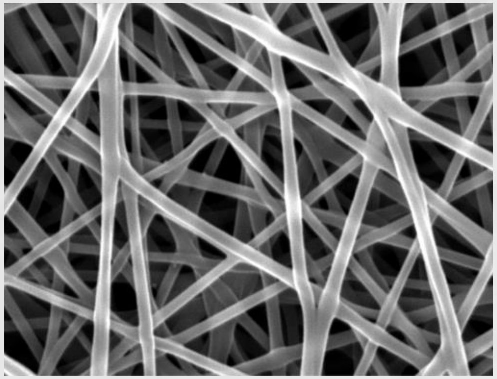
C_f : Floating cells

C_s: Seeded cells

Cell: MC3T3-E1 osteoblast-like cells

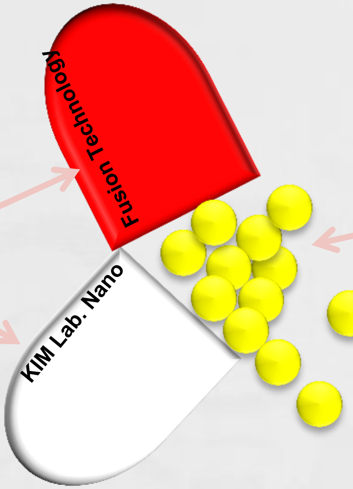
Biomedical Application: Drug Delivery System

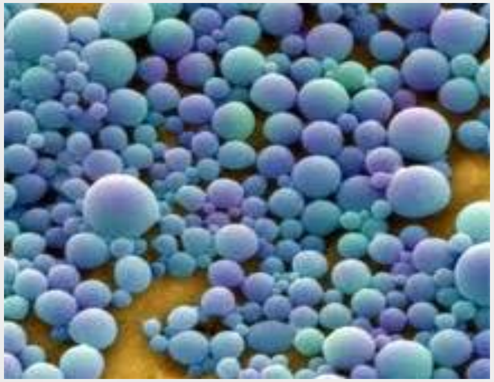
•**Nanotechnology** **has been utilized to develop new therapies and next generation nanosystems for "smart" drug delivery.**



Nanofibers

- To enhance the therapeutic activity by prolonging drug half-life
- To be released through diffusion system

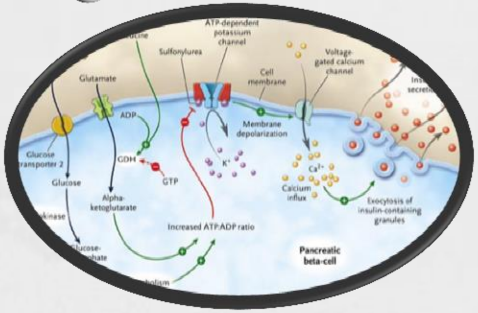




Nanoparticles

- Improving solubility of hydrophobic drugs
- Reducing potential immunogenicity

In vivo
•Glucose reaction



Biomedical Application

•Why not using oral drug ?

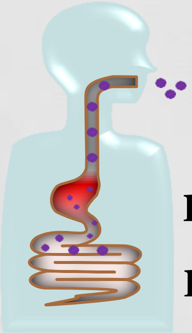
•Get denatured readily by low pH of gastric medium in the stomach.

•Different digestive enzymes in the stomach and small intestine may lead
to degradation of peptide/protein drugs

Injection type

Painful and inconvenient : thus leading to low patient compliance

Needs
Future Drug Industry
60% occurs



pH 1.2-2.5

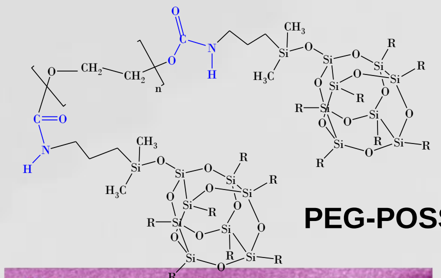
pH 7-8

Oral type

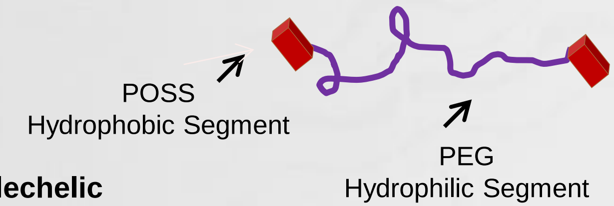
Most convenient and comfortable

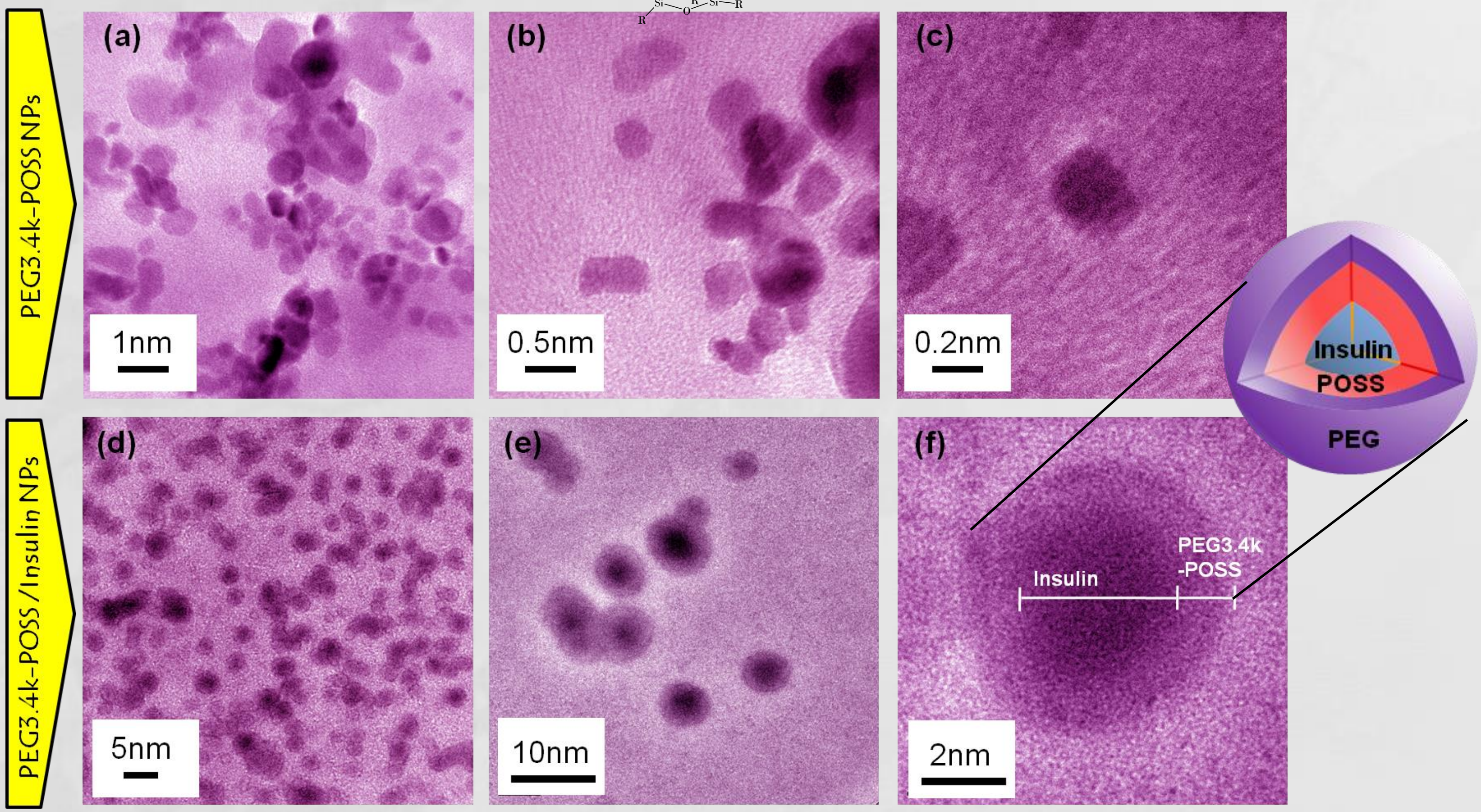
Biomedical Application: Nanoparticles

Core-Shell Nanostructured Particles



PEG-POSS Telechelic

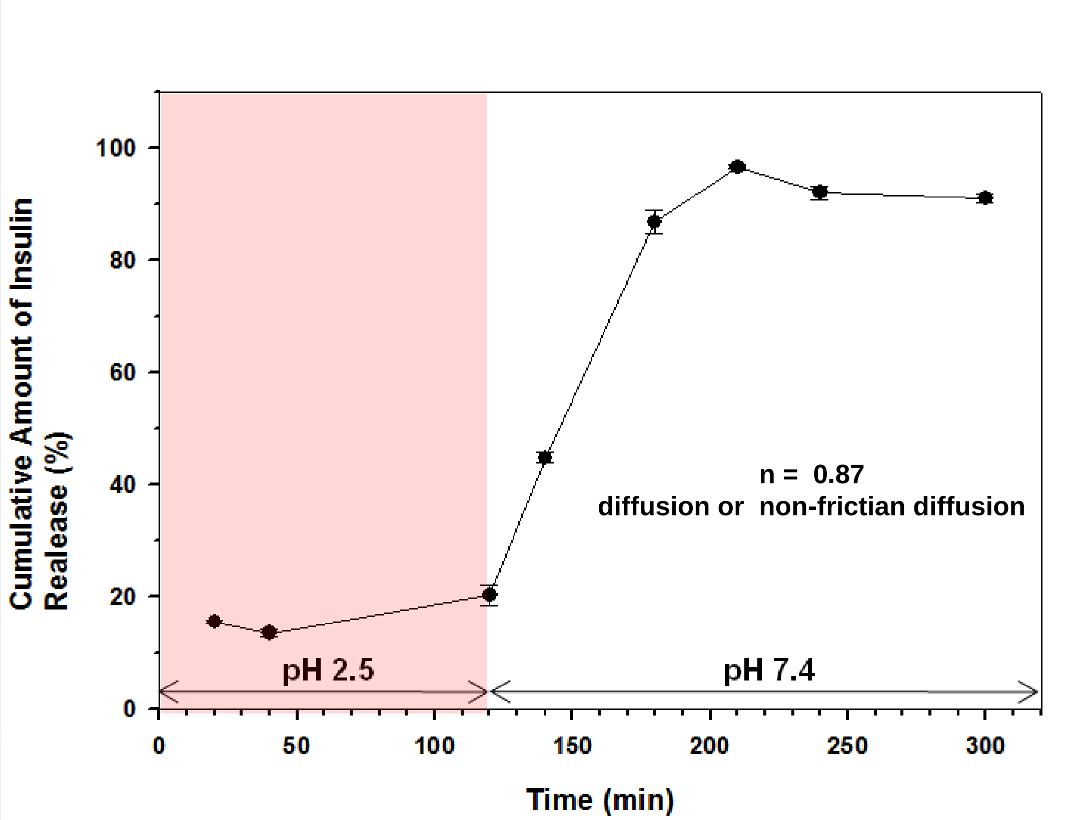




K. O. Kim, Y. A Seo, B. S. Kim, K. J. Yoon, M. S. Khil, H. Y. Kim, I. S. Kim, *Colloid. Polym. Sci.* **2011**, *289*, 863-870.
K.O. Kim, B.S. Kim, I.S. Kim, *J. Biomater. and Nanobiotechnol.*, **2011**, *2*, 201-206.
B. S. Kim, P. T. Mather, *Macromolecules* **2002**, *35*, 8378-8384; *Macromolecules* **2006**, *39*, 9253-9260.

Biomedical Application: Nanoparticles

- ***In-vitro* Insulin Release Behavior**



- ***Diffusion controlled mechanism***

The drug release behavior according to diffusion controlled mechanism is usually governed by the following equation,

$$M_t/M_\infty = kt^n$$

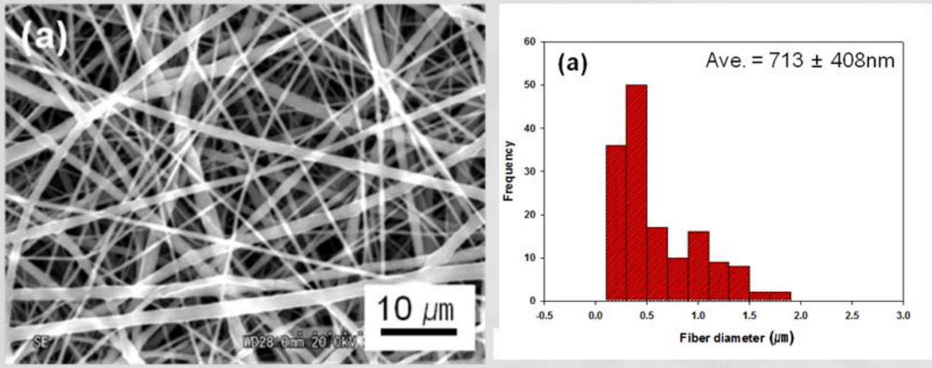
where M_∞ is the total amount of insulin in dosage form, M_t is the amount of insulin released at time t, k is kinetic constant, and n is diffusion or release exponent constant.

K.O. Kim, B.S. Kim, I.S. Kim, *Journal of Biomaterials and Nanobiotechnology*, **2011**, *2*, 201-206.

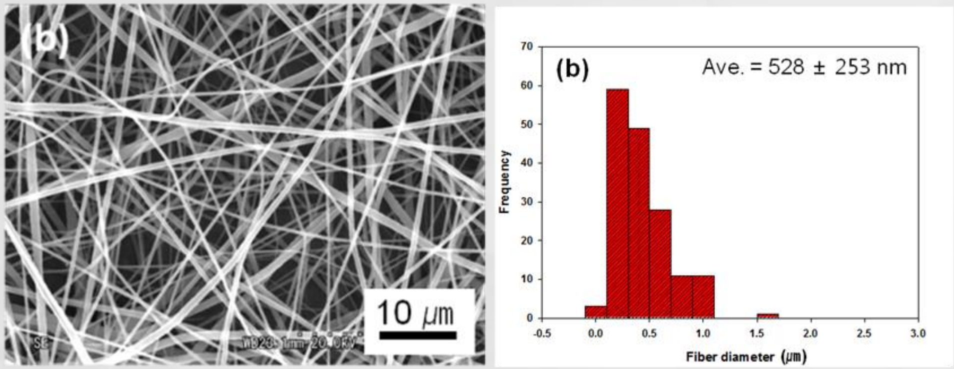
Biomedical Application: Nanofibers

Morphologies of PCL/PEG-POSS nanospun scaffolds

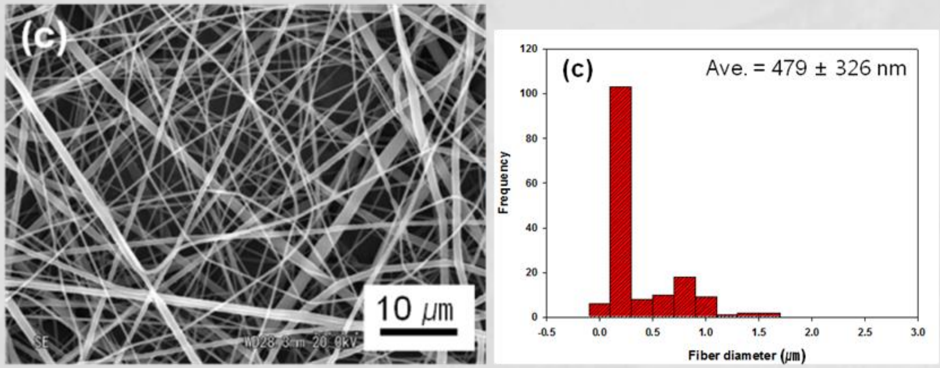
PCL



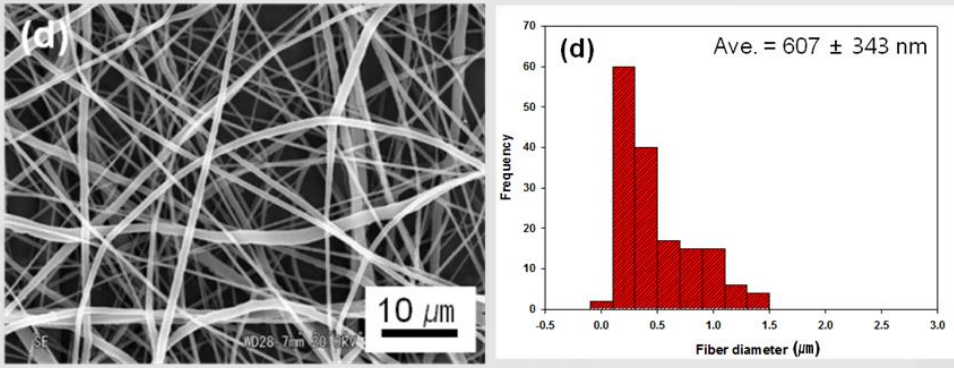
PCL/PEG3.4k-POSS



PCL/PEG8.0k-POSS



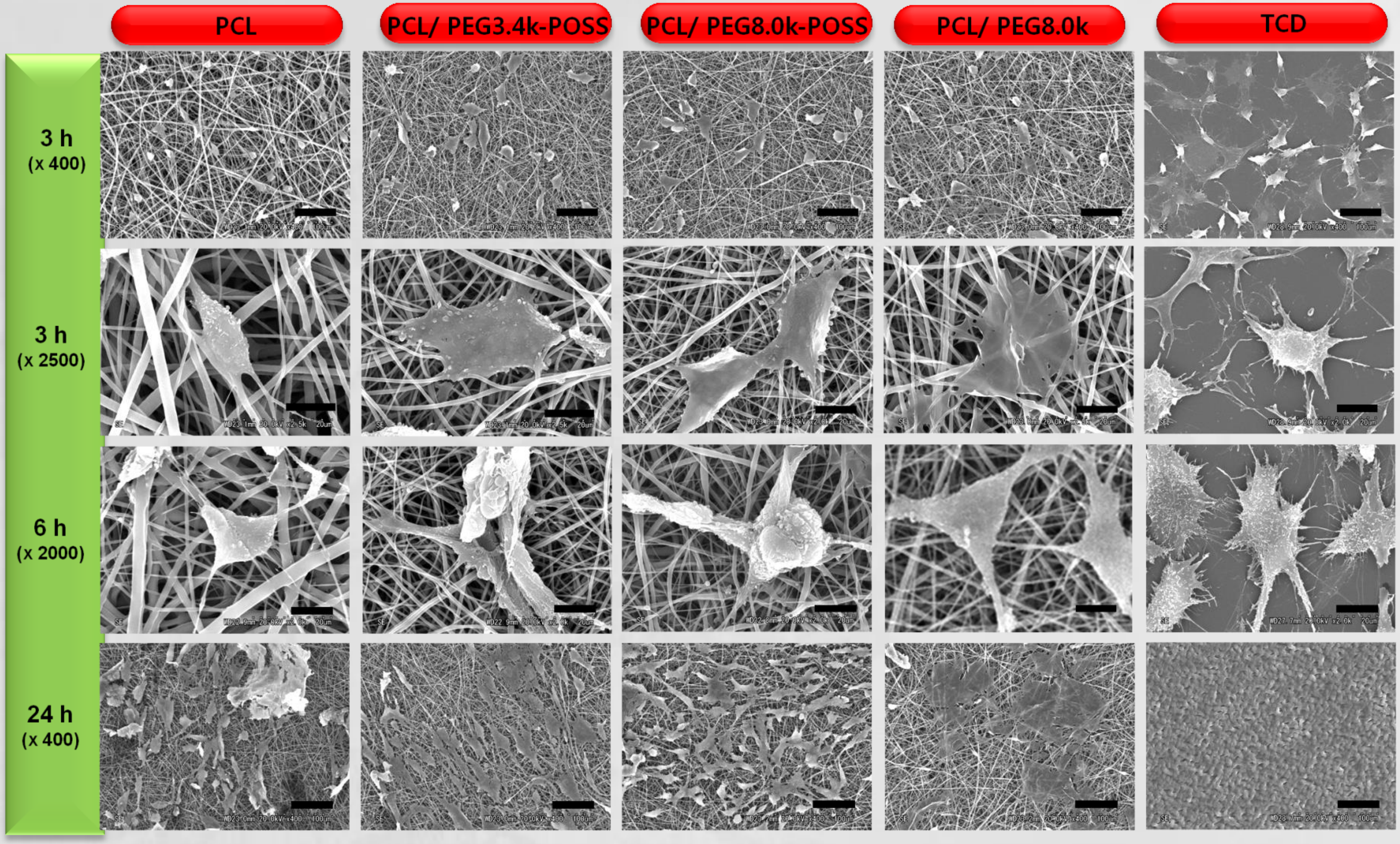
PCL/PEG 8.0k



K.O. Kim, B.S. Kim, I.S. Kim, to be submitted (2011).

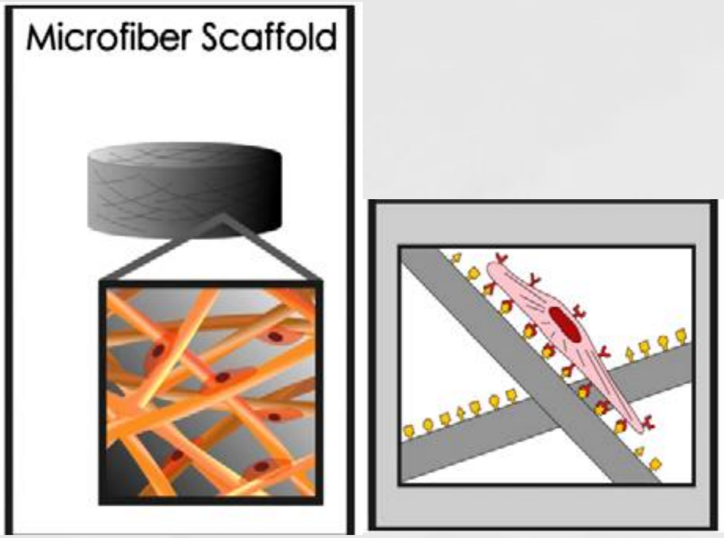
Wettability of PCL/PEG-POSS Nanospun Scaffolds

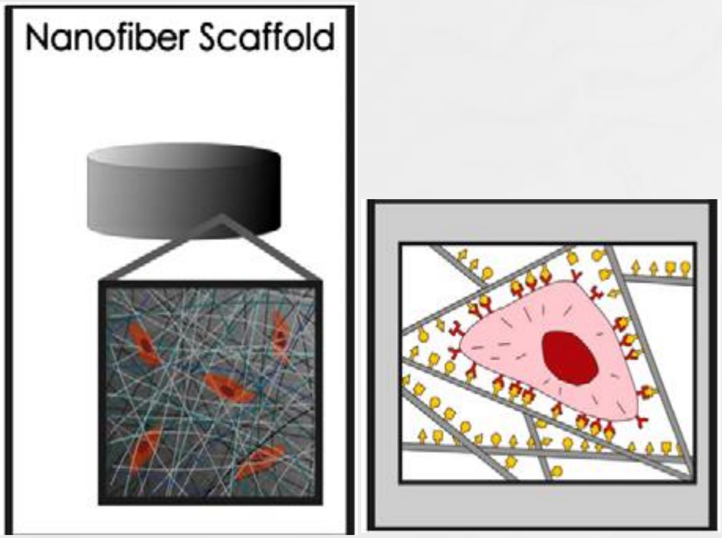
SEM Images of Cultured PCL/PEG-POSS Scaffolds

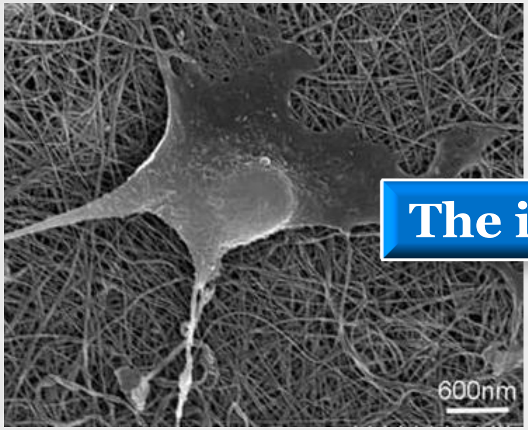


- The behaviors of MC3T3-E1 cells are influenced by the wettability of Scaffold
- The PCL/PEG3.4k-POSS and PCL/PEG8.0k-POSS electrospun webs showed significantly higher attachment ability, good activity of the cells than pure PCL web

3D Nanofibrous Scaffolds for Cell Culture

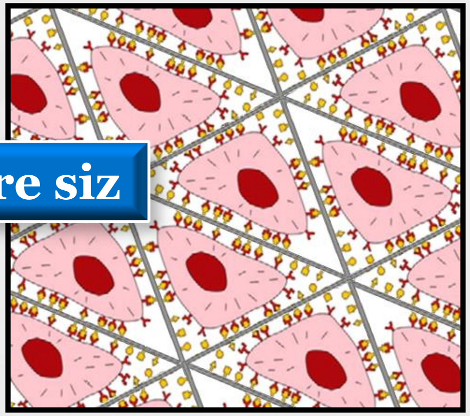






Kai Wei, Yuan Li, Kyu-Oh Kim, Yuya Nakagawa, B young-Suhk Kim, Koji Abe, Guo-Qiang Chen, Ick-Soo Kim.
JOURNAL OF BIOMEDICAL MATERIALS RESEA RCH PART A. 2011

The increase in pore siz
e



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(Chonbuk Nat'l Univ., Korea)

Dr. Kai Wei, Dr. Yuan Li (Shinshu Univ., Japan)
Ms. Kyu-Oh Kim (Shinshu Univ., Japan)
Ms. Akada Yaeko (Shinshu Univ., Japan)

All members, Nano Fusion Technology Research Lab.


Thank you very much
for your attention!