ME221 – Structural Materials
Group 1 : Artificial Skin - Biomedical

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What all is covered ?

- Introduction to Artificial Skin
- Anatomical overview of Human Skin
- Perception of Human Skins
- Requirement of Artificial Skin
- How Artificial Skin is Made ?
- How Artificial Skin works ?
- Why Artificial Skin is better than Skin Grafting ?
- Challenges
- Future Prospects

Introduction

An artificial skin is defined to be a material or a device that is applied on the patient's body to substitute, mimic or improve any skin function

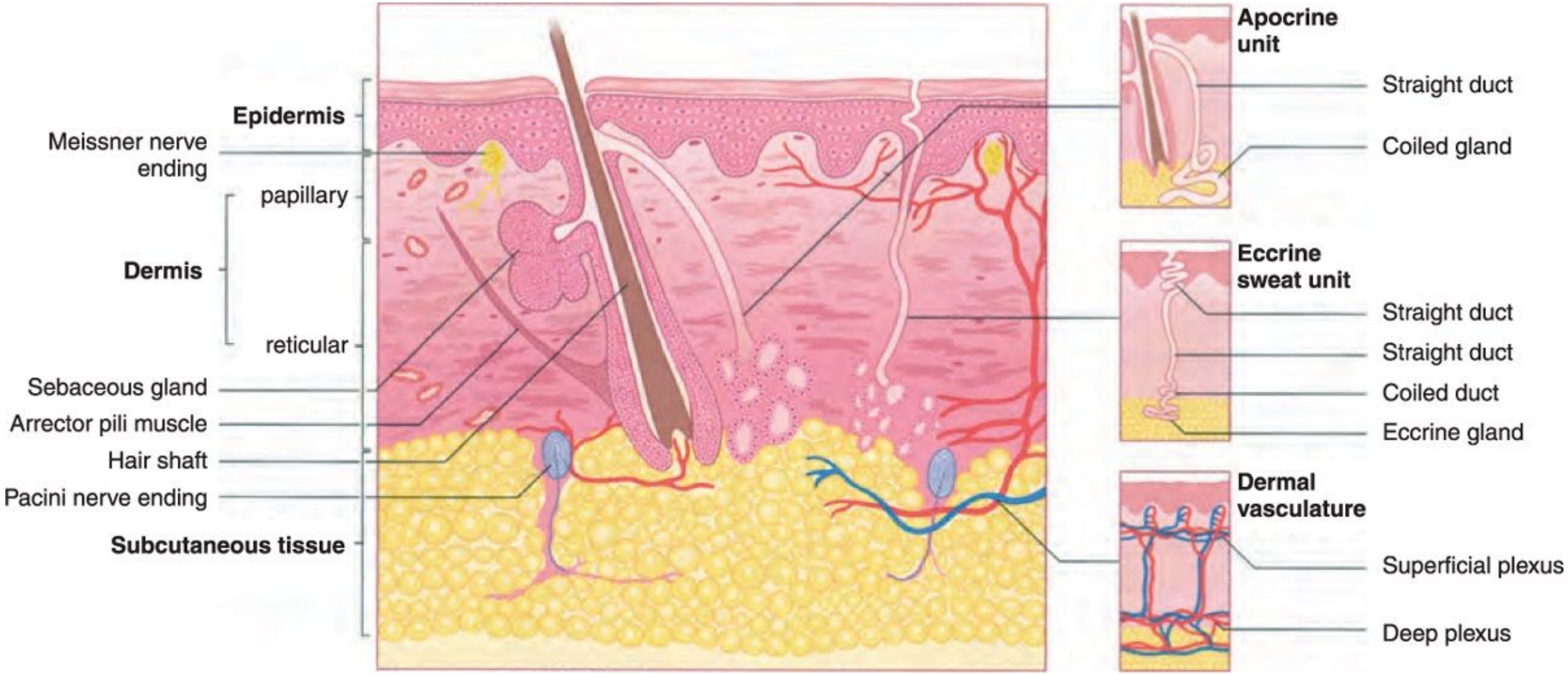
The materials need to be carefully selected to ensure proper integration with host tissue without triggering an immune response

The skin is required to be biocompatible, porous, flexible, skin-mimicking, and cost-effective to smoothly imitate natural skin

Artificial skin can revolutionize medicine with its lifelike and functional substitutes

Anatomical Overview of Human Skin

- The skin is composed of three layers: the Epidermis, the Dermis, and Subcutaneous tissue.
- The **Epidermis does not contain blood vessels**; cells in the deepest layers are nourished by diffusion from blood capillaries that are present in the upper layers of the dermis.

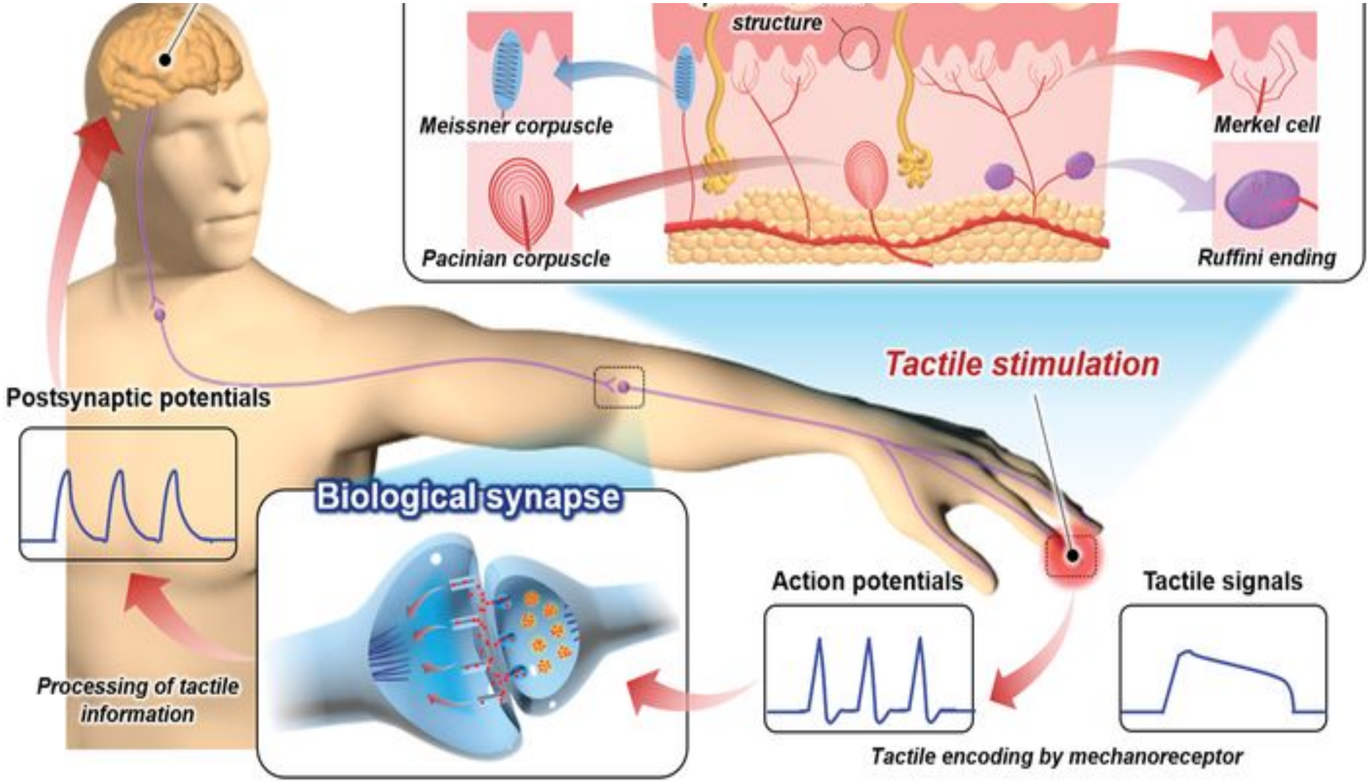


Cross-Section of Skin and Panniculus. Note. From Andrews' Diseases of the Skin: Clinical Dermatology (10th ed., p. 1), by W.D. James, T.G. Berger, and D.M. Elston, 2006

Human Skin Perception

Types of Receptors in Human Skin -

- Mechanoreceptors (pressure or distortion)
- Nociceptors (pain)
- Thermoreceptors (temperature)



Human tactile perception system.

Lee, Youngoh & Park, Jonghwa & Choe, Ayoung & Cho, Seungse & Kim, Jinyoung & Ko, Hyunhyub. (2019). Mimicking Human and Biological Skins for Multifunctional Skin Electronics. Advanced Functional Materials. 30. 1904523. 10.1002/adfm.201904523.

Requirements of Artificial Skin

Artificial Skin can be used in the following domains :

- **Medical**
  - For the aid of burn victims and patients with chronic wounds
  - To provide realistic training mechanism to medical students
  - To enhance the appearance of an individual ie. cosmetic surgeries
  - To regain the sense of touch for physically handicapped people with prosthetics
- **Research & Development**
  - To test it with harsh weather and external conditions to protect astronauts in space
  - To allow robots to interact with their environment more effectively
  - To better understand skin diseases and develop effective treatments

Applications of Artificial Skin

INTEGRA :

Integra is used to help heal large wounds where skin has been injured and/or needs to be regrown.

The top layer, made of thin silicone sheet, protects the patient from infection and dehydration.

The bottom layer, made of several layers of Collagen, Chitosan and Gelatin, acts as scaffolding where new skin will grow.Compared to traditional skin grafts, the use of Integra reduces pain and scarring.

Fabrication Methods

3D Bioprinting[7] :

Steps involved:

- Pre-processing- Tissue imaging, Model design, Bioink prep
- Processing- **Bioprint** target biological tissue
- Post-processing- Printed cells to proliferate and differentiate

Bioink- A solution or hydrogel composed of biomaterials, living cells and biologically active factors.

Biomaterials present include chitosan, collagen etc.

BIOPRINTING

Laser-assisted

- ➢ Laser-induced forward transfer
- ➢ Maximum activity of bioink

Inkjet

- ➢ Like 2D inkjet printers
- ➢ Thermal/piezo electric
- ➢ Pulse pressure by either heating or voltage change

Extrusion

- ➢ Uses compressed air
- ➢ Continuous line deposition

Fabrication Methods

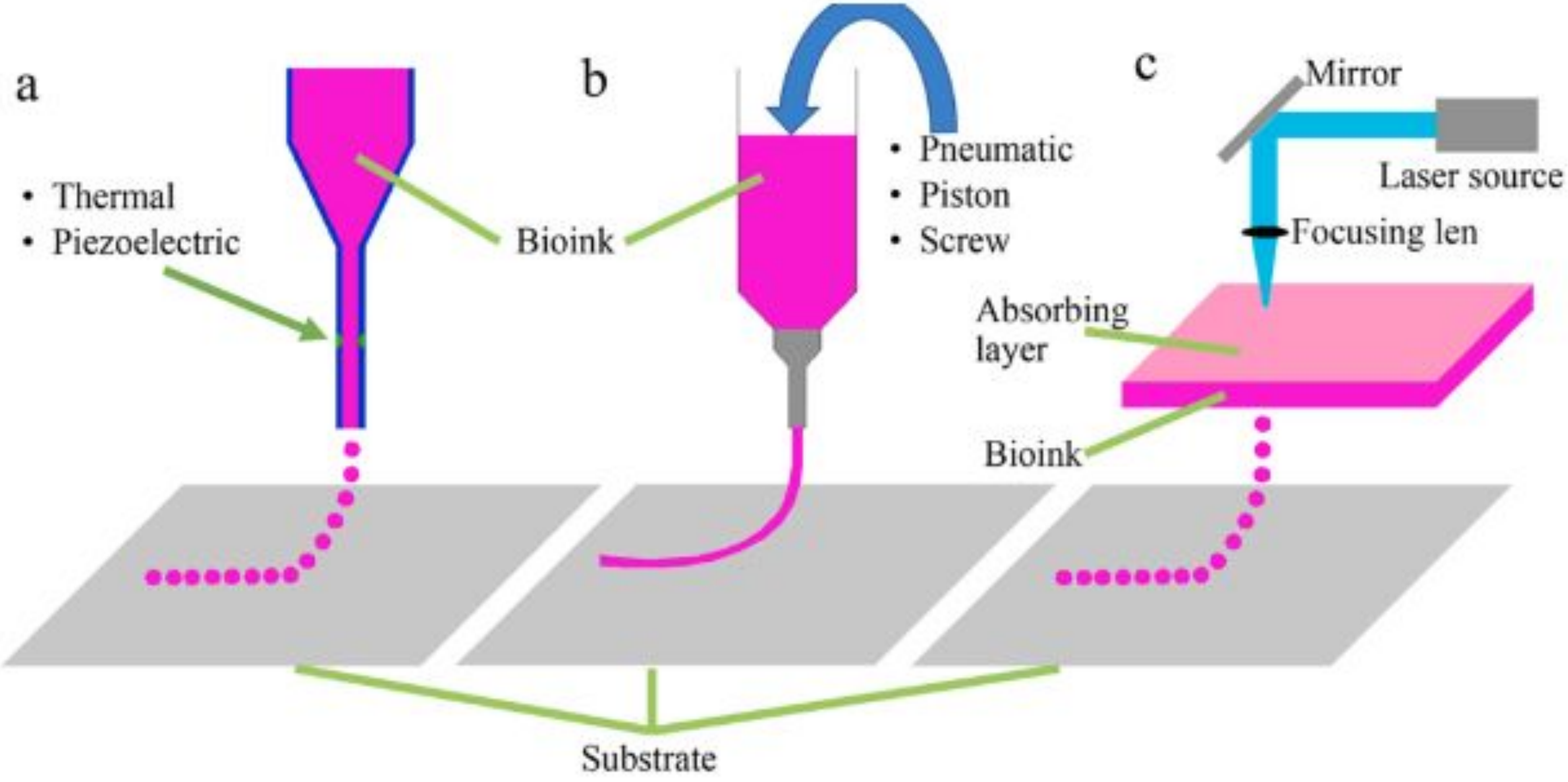


Fig. 3. Three main bioprinting strategies. (a) Inkjet printers with a thermal or piezoelectric actuator; (b) extrusion printers use pneumatic or mechanical (piston or screw) dispensing systems; (c) laser-assisted printing.

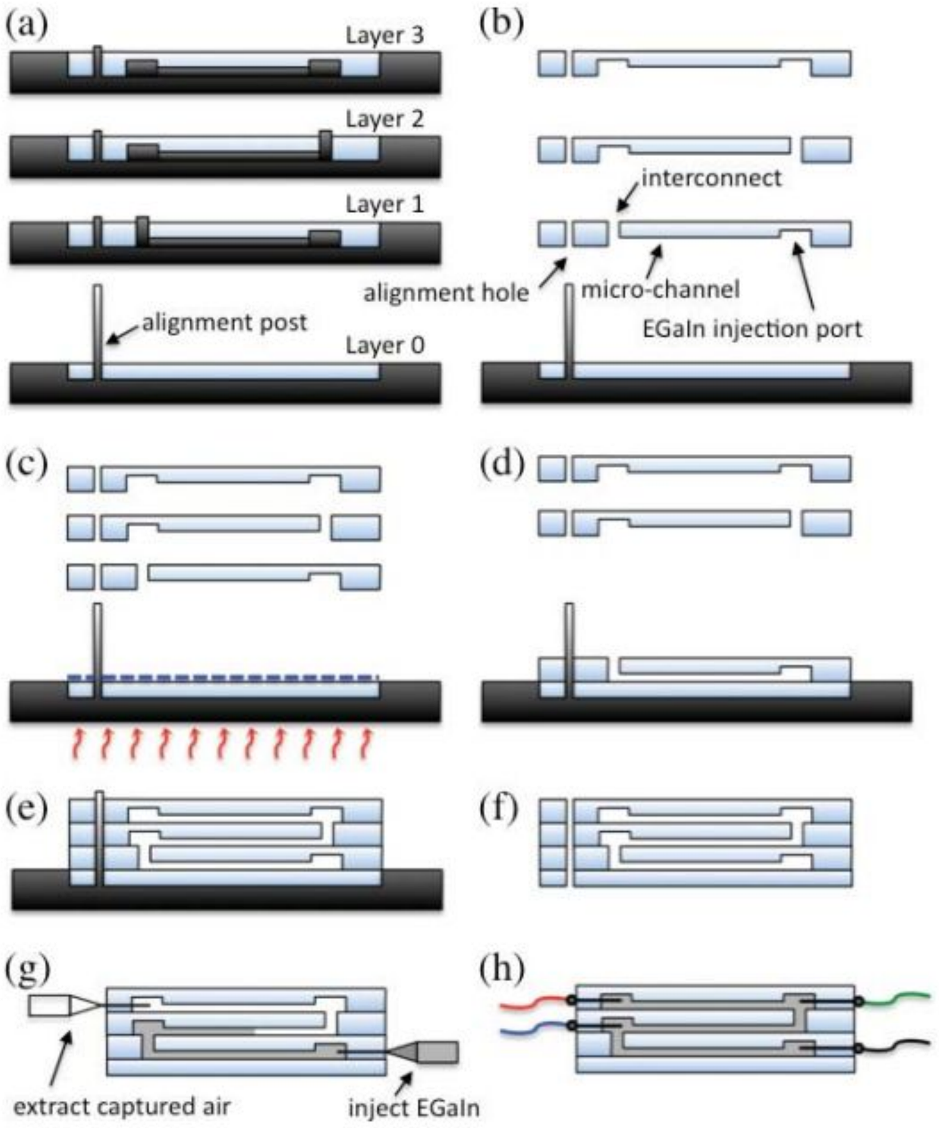
3D bioprinting for fabricating artificial skin tissue (2021) Chuang Gao a, Chunxiang Lu a, Zhian Jian a, Tingrui Zhang b,d, Zhongjian Chen c,d, Quangang Zhu c,d, Zongguang Tai c,d, Yuanyuan Liu a,*

Fabrication Methods

Fabrication of Artificial Skin Using Embedded Microchannels and Liquid Conductors [8]:

- The method is used for fabrication of electronic components in skin.
- The sensor prototype was fabricated using a layered molding and casting process, the base material is Silicone rubber chosen for high stretchability.
- Plastic molds are prepared using a 3-D printer.
- The cured layers are bonded by spincoating the same liquid silicone between the layers.
- In each bonding step, alignment is important to ensure the channel connection between layers through the interconnects.
- In the final step, EGaIn3 is injected into the microchannels using two syringes. One syringe injects EGaIn, and the other syringe extracts air captured in the microchannels.
- Finally, wire connections are made by inserting electrodes.

Fabrication Methods



Fabrication process. (a) Prepare molds and pour liquid silicone. (b) Remove molds when the silicone cures. (c) Spin-coat Layer 0 (2000 rpm for 50 s.) and partially cure (60 °C for 1 min.). (d) Bond Layers 1 to 0. (e) Bond Layers 2 and 3 by repeating spin-coating and partial curing. (f) Remove mold of Layer 0. (g) Inject EGaIn using syringes. (h) Connect wire by inserting electrodes.

Design and Fabrication of Soft Artificial Skin Using Embedded Microchannels and Liquid Conductors (2012), Yong-Lae Park, Member, IEEE, Bor-Rong Chen, Member, IEEE, and Robert J. Wood, Member, IEEE

Growing the matrix

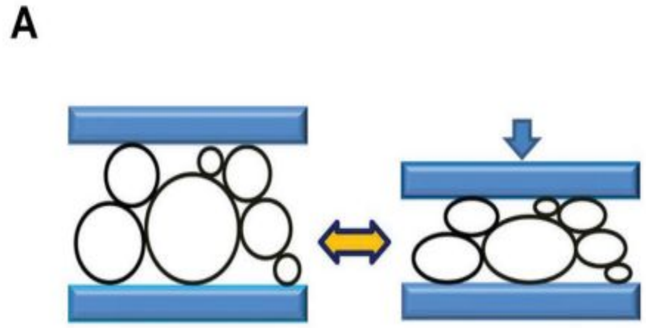
- The matrix in artificial skin serve as foundation for creating a structure that can closely mimic the mechanical and functional properties of the skin.
- We can use natural or synthetic materials to create the matrix.
- Natural materials include **chitosan**, **silk fibroin**(can be processed into nanofibers matrix) and **collagen**(can be processed as nanofibres or 3d printed constructs) etc.
- We can also have hybrid of two or more polymers to have superior properties as skin for e.g. **HAMA(methacrylated hyaluronic acid)**, **GeIma(methacrylated gelatin)** and **konjac glucomannan** etc.
- Synthetic polymers include Polyurethane, Polyvinyl alcohol and **PLGA**(poly lactide-co-glycolide) etc.
- An outer layer of silicone is normally applied to the matrix in order to serve as a protective layer.

Materials used for Artificial skin

- Since skin is a **sense organ** we need to have sensing as prime feature in the artificial skin which involves pressure and temperature sensing.
- For pressure sensing we have two types of materials:

1. **Piezoresistive materials**- Piezoresistive sensors allow the measurement of strain from a change in resistance.

- **Polypyrrole (PPy) hydrogel array of hollow-spheres** is used.
- After application of pressure contact area is increased which results in change of contact resistance.
- This results in detection of pressure less than 1 Pa.



Artificial skins possessing piezoresistive properties. (A) Strain causing a variation of electrical contact between the electrode and hydrogel made from polypyrrole (PPy). Recent innovations in artificial skin Zhi Wei Kenny Low, a Zibiao Li, a Cally Owh,a Pei Lin Chee (2019)

Materials used for artificial skin

2. **Capacitive Materials**- The basic principle relies on the fact that the distance between two conductive layers changes when pressure is applied, leading to change in capacitance.

- Materials used for **temperature sensing**-
  - Temperature sensors replace thermoreceptors in the skin
  - In this we use stretchable temperature sensor array consisting of polyaniline nanofibers electrochemically polymerized onto poly(ethylene terephthalate) (PET) films.
- **Flexibility** is also one of the important aspect of the skin.

  To impart flexibility and mechanical strength into artificial skins we have some materials such as:
  - soft substrates such as silicone rubbers
  - Graphene and graphene-based materials
  - Hydrogels
  - Polyurethane
  - Shape memory polymers

SKIN GRAFTS

Skin Grafts are skin patches removed from healthy skin areas and pasted onto damaged areas while in case of artificial skin, new skin is made by growing cells.

Surgical removal (excision or debridement) of the damaged skin is followed by skin grafting.

Types of Skin Grafts by Donor and Recipient : Autogeneic, Isogeneic, Allogeneic, Xenogeneic

Artificial Skin is better than Skin Grafts :

If taken from the same person, then it creates a secondary wound.

If taken from different individual / species, then high chance of rejection

SKIN GRAFTS

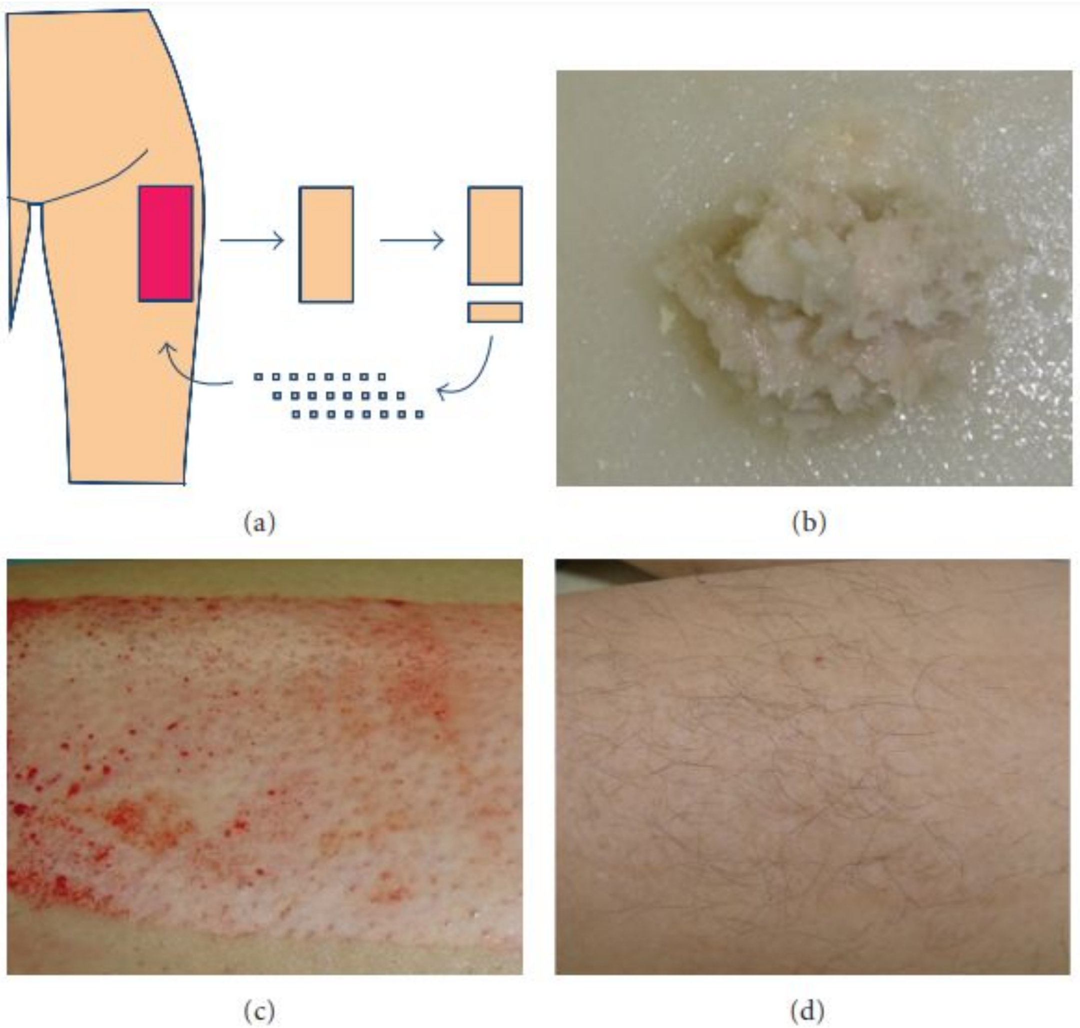


Image of recruited minced skin grafting (a), and minced skin (b). The donor site before minced skin was transplanted (c). One year after minced skin grafting (d). Scar is almost invisible.

Ruka Shimizu and Kazuo Kishi(2011), Skin Graft, Department of Plastic and Reconstructive Surgery, Keio University

Challenges for Artificial Skin

Biocompatibility :-

- Several problems can arise during implant of Artificial Skin over body like mechanical stress and regeneration of skin leads to extrusion out of body.
- Immunogenic responses results in inflammation and fibrosis around the implant.
- These responses are triggered by factors like inherent chemical and physical properties of material, mechanical agitation on surrounding tissues and toxic leachables from the implant.
- Harsh environment of Human body can damage the device.

Challenges for Artificial Skin

How is Biocompatibility tested ?

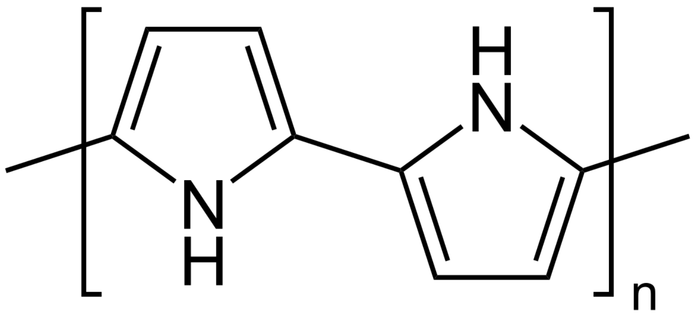
- Both in vitro and in vivo tests are used in accordance with guidelines such as the ISO 10993.
- In vitro tests investigate at the response of isolated cells to toxic agents. While these tests are easier and more convenient, they are not able to provide evidence of the body's response to an implant.
- There is still a need for implantation, or in vivo, tests to investigate the physiology of the implant site.

Challenges for Artificial Skin

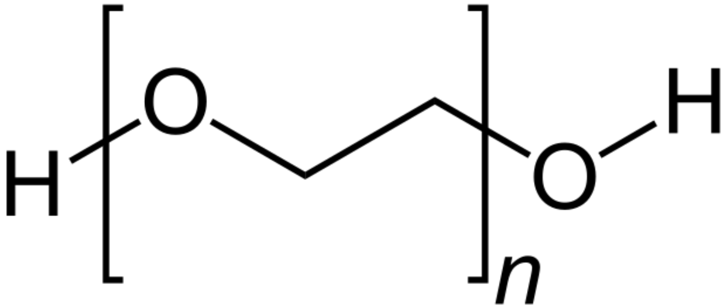
Tackling the issue of Biocompatibility :-

- Using biocompatible materials like PPy(PolyPyrrole), and poly(3,4-ethylenedioxythiophene) (PEDOT) have been used for biocompatibility enhancement.
- Similarly, flexible yet biocompatible polymeric films such as polyimide[2], cellulose[3], and silk fibroin[4] may be substitutes for substrate materials.
- Coating the device to protect fragile components while creating a desirable interface between the device and tissue.
- One common material used in coatings is poly(ethylene glycol) (PEG), a biocompatible polymer well-known for its low protein-adsorbing properties,[5] which can be used to prevent a foreign body response .

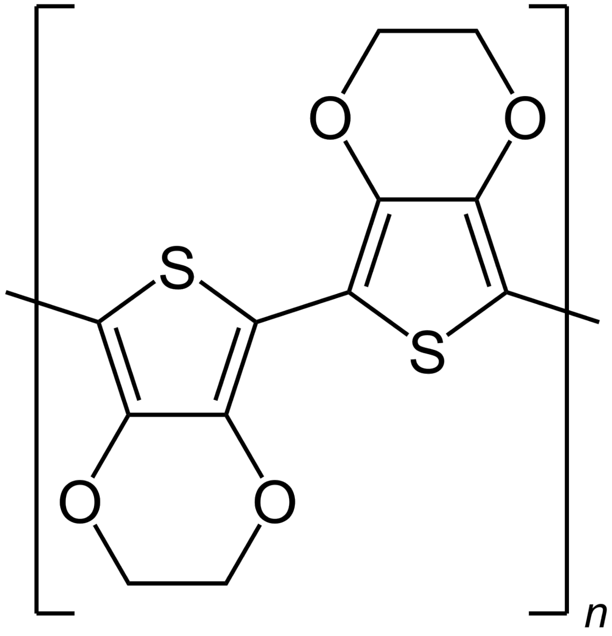
Structure of materials used



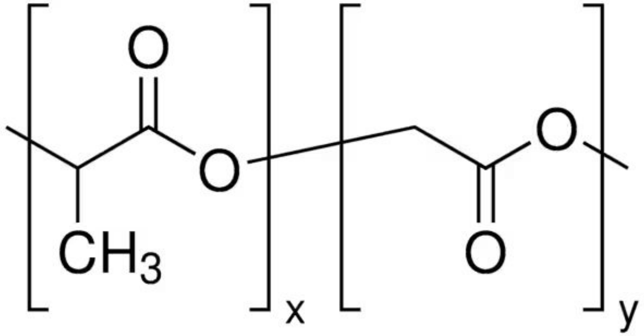
PolyPyrrole



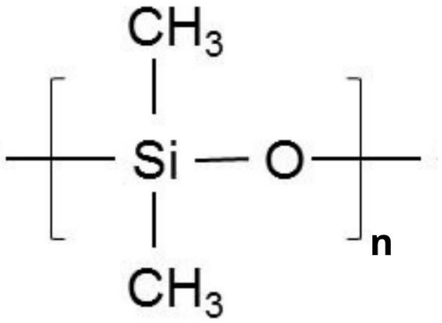
Poly Ethylene Glycol PEG



PEDOT



PLGA(poly lactide-co-glycolide)



Structure of a silicone polymer

Future Prospects

- Absolute Sensory Perception
  - ❖ Neural Interfacing Systems
  - ❖ Optogenetics/ Magnetic stimulation
- Second Skin
  - ❖ Electronic Epidermal Systems(EES)
  - ❖ Monitoring Life activities
  - ❖ Aesthetics
- Camouflage
  - ❖ Photonic/Optoelectronic Skins
  - ❖ User-interactive
- Smart Skin
  - ❖ Change in pH and temperature
  - ❖ Solar radiation protection
  - ❖ Cell sheet engineering

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