
# PHYSICAL CHEMISTRY

## Take Home Final

Melt-Electrowriting Methodology for Additive Manufacturing and biofabrication

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# Introduction

## Additive Manufacturing (AM):

The term "additive manufacturing" refers to a set of techniques that are used to rapidly and affordably create a scale replication of an original product or assembly. One of the most recognized uses of additive manufacturing techniques is quick prototyping. AM is the term most commonly used to describe 3D printing in manufacturing. There are two similar AM techniques recently used in advanced synthesis of biological structures, Melt Electrowriting and Melt Electrospinning.

## What is Melt Electro writing (MEW)?

Melt electro writing is a technique which uses microfiber polymers to create structures with the help of computers. It is similar to 3D printers, but the main differences are MEWs are way more precise it is up to nanometer-micrometer range and can use biologically compatible fibre. A standard MEW device has one nozzle which uses high voltage to soften polymer for precision. With this way layer by layer, we can design and produce very precise bioorganic or polymeric substances to use in industry and medical areas.

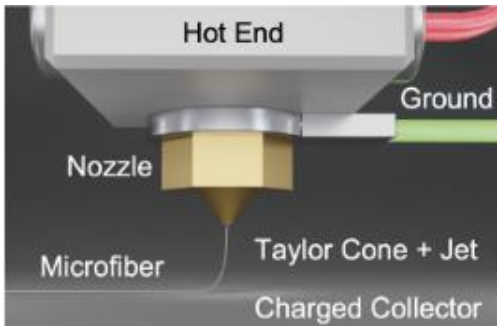


*Figure 1: Nozzle Structure of MEW*

## Melt Electrospinning (MES):

Melt Electrospinning is a method which generates continuous fibers in the form of a liquid jet from a polymer solution or melt using electrostatic force. Electrospinning is based on the electrohydrodynamic (EHD). MEW and MES are both works a like 3D printer main differences are, in MES this method fibers synthesized randomly and collected by collector board while MEW is synthesizing and precisely places the fibers to needed structures just like writing.

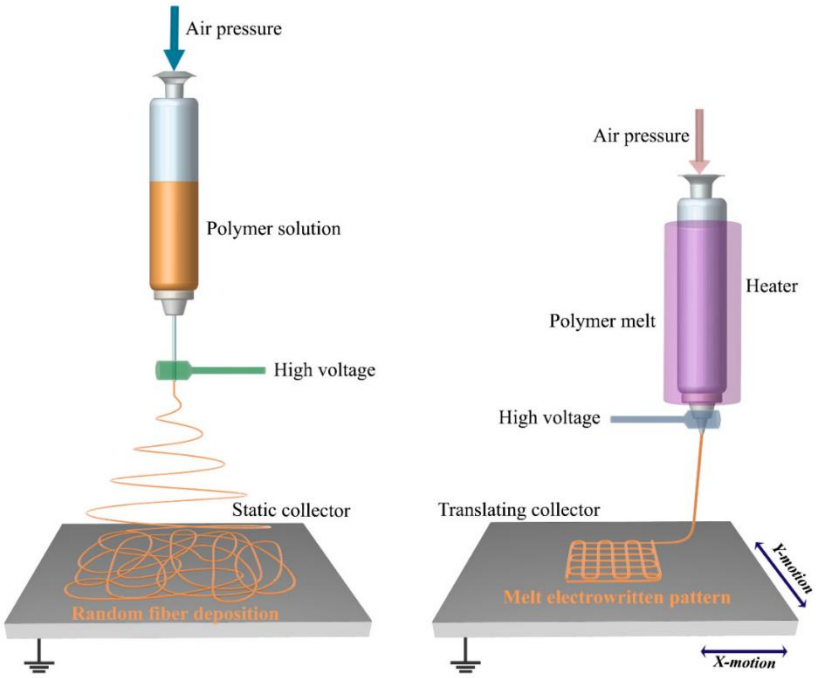


*Figure 2: Difference between MES and MEW.*

*The one on the left side is MES and the one on the right side is MEW.*

## Methods

### Which structures can we use as MEW and MES filaments?

- Polycaprolactone (PCL): PCL is the most important filament in MEW because of its quick solidification, minimal degradation, low melting temperature, and biocompatibility, PCL, a hydrophobic polyester, is a great option for the MEW process.
- Polylactic acid (PLA): The cytocompatibility and biodegradability of PLA, a synthetic polyester, have made it a sought-after contender for a variety of uses in tissue engineering and biomedicine. For tissue engineering purposes, several research have employed PLA scaffolds created using various methods, such as electrospinning.
- Polypropylene (PP): PP demonstrates strong long-term durability and is often utilized in medical equipment.
- Thermoplastic Polymers: These polymer chains specifically interact via intermolecular interactions, which rapidly decrease when a higher temperature is applied, resulting in a viscous liquid that may be used to create microscale fibers with excellent control. The majority of thermoplastics usually have large molecular weights, which increases the

degree of chain entanglement needed to produce a jet at the low mass flow rates necessary for MEW. It is not strongly recommended filament but also it can be useful in some industries or specific structures.

- Others: There are lots of different filaments in use; modified PCLs, polialirate, polyethylene etc. They all have different active temperatures, diameters for specific usage.

**MEW-MES Configurations:**

Before we talked about MEW and MES devices works just like each other, this time we will discuss how to set them up to work optimally.

A) Applied Voltage

These AM devices uses with electrical potential to soften or activate the substance to turn it to fiber form. Generally, 4 to 12 kV voltage used for PCL (mostly used filament) while some substances work at 120 kV voltage. Applied voltage can change the diameter of fibers and precision of writing.

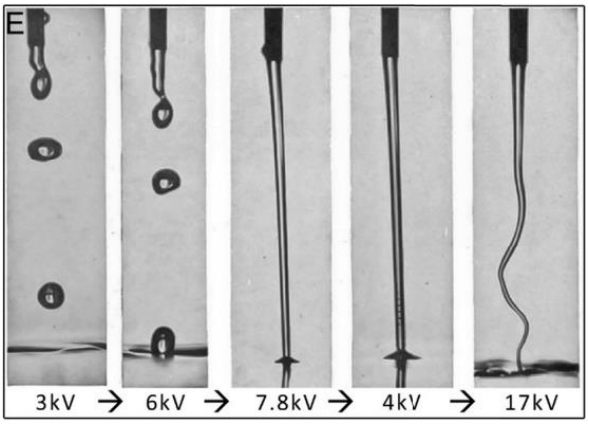

*Figure 3: Effect of Applied Voltage on water column.*

B) Flow Rate

Flow rate is proportional to voltage and diameter of fiber. The more we increase the flow rate, the more we have to increase the voltage to get the best result.

C) Collection Distance

Most of the research rely on a relatively short nozzle to collector board distance as compared to solution electrowriting. Typically, collection distances of 3-5 cm have been used, and according to certain laboratories, the collection distance and fiber diameter are connected.

D) Heating and Cooling

One of the most important things in MEWs is heating and cooling process. Without heating the filament or liquid can not reach its optimum form. To achieve optimal results both heating and cooling should be on point. Heating is important to shape of filament (diameter or any structural) and cooling is important for stability and precision. There are four different types of heating in MEW: Heated air, laser source, electrically heated and rotating fluids model.

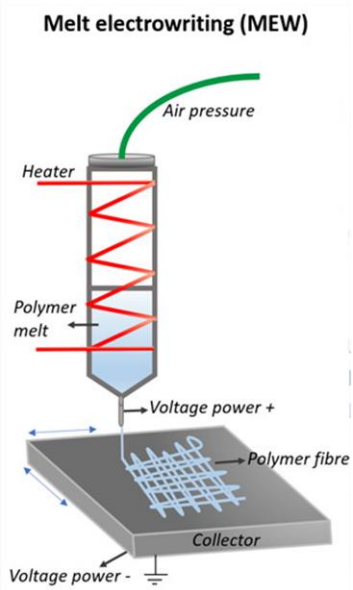


*Figure 4: MEW with Rotating fluid heater.*

## Applications and Products

**Tissue Engineering:** The goal of the scientific field of tissue engineering (TE) is to create implantable materials that can be used to cure illnesses and injuries in a secure way. Therefore, in order to produce a successful and medically proper tissue build-up, TE must combine multiple areas such as cell biology, material science and a highly complicated bioreactor design. Implantable matrix structures, also known as scaffold structures, are frequently required to guide cell ingrowth, differentiation, and tissue creation as well as an ideal adaption in a host tissue in order for TE products to be successful in repairing and regrowing damaged tissue. Here is some examples for tissue engineering with different resources in Table 1.

| Tissue | Scaffold description | Citation |
|---|---|---|
| Myocardial Tissue | Hexagonal PCL microstructure | Castilho et al. (2018) |
| | Rectangular or square pore (poly (hydroxymethylglycolide-co-ε-caprolactone) scaffolds | Castilho et al. (2017) |
| Heart valve | Serpentine PCL architecture to mimic collagen fibers | Saidy et al. (2019) |
| Ligament and Tendons | Sinusoidal patterns for aligned, crimped collagen fibrils imitation | Hochleitner et al. (2018a) |
| Skin | PCL blend with bioactive milk proteins to promote cell growth, spreading infiltration | Hewitt et al. (2019) |
| Bone | Poly (lactic acid) scaffolds with square pores | Meng et al. (2021) |
| | PCL MEW with square pores and chaotic gelatin SES scaffold | Wang et al. (2021) |
| | Calcium phosphate coated PCL scaffolds with square pores and fiber offset | Abbasi et al. (2020) |
| Cartilage | PCL structures with square pores for cell laden hydrogel reinforcement | Peiffer et al. (2020) |
| | PCL structures with square pores in combination with cytokine loaded PLGA microspheres | Han et al. (2020) |
| | Reinforced hyaluronic acid scaffold MEW PCL structure with square pores | Galarraga et al. (2021) |
| Blood vessel | Tubular PCL scaffold with square pores with aortic root features | Saidy et al. (2020) |
| | PCL electrospinning (chaotic) and MEW (rectangular pores) bilayered scaffold | Jungst et al. (2019) |
| Periodontal Tissue | PCL scaffolds with square pores with fluorinated calcium phosphate caoting | Daghrery et al. (2021) |
| Nerve tissue | Gold coated PCL scaffold with square pores | Wang Y et al. (2020) |
| | PCL scaffold with square pores and different surface modifications | Chen T et al. (2021) |

*Table 1: Examples from tissue engineering with MEW according to Loewner et al. 2022*

**MEW products form different filaments:** Nowadays, there is many MEW-compatible filaments and polymers available and they can be used to design. We can synthesize different and specific to material structures with the help of MEW device. In figure 5 there is twelve different filaments and structures created with MEW method.

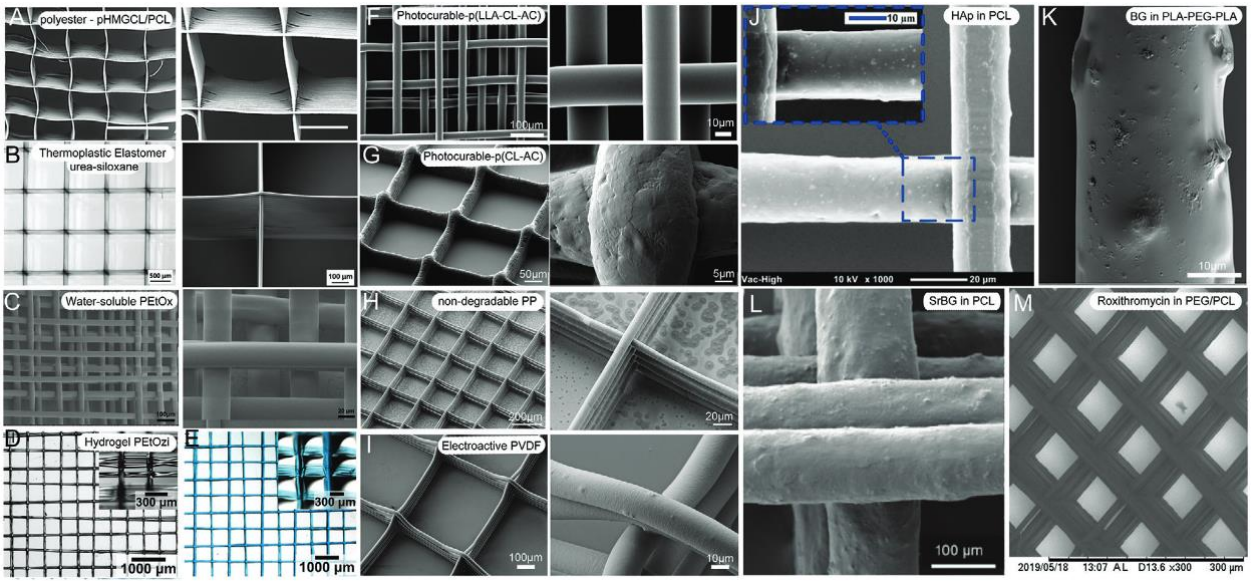


*Figure 5: MEW product examples from different filaments in scanning electron microscope. Kade, J. C., Dalton 2020*

| Polymer class | | Fiber diameter [μm] | Layers | Nozzle diameter [Gauge] | Temperature [°C] | Voltage [kV] | Pressure [bar] | Speed [mm min$^{-1}$] | Distance [mm] | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| Polyesters | pHMGCL/PCL 40:60 | 3–7 | 25–30<br>200 × 200 μm<br>150 × 300 μm | 27 | 84 | 5–8.5<br>5 | 1–4<br>2 | 600–2400<br>300 | 3–5<br>3 | [84] |
| | Poly(urea-siloxane)s; thermoplastic elastomer | 10.6 ± 0.6 to 19.5 ± 1.5 | 100<br>50 in *x*/*y* | 24 | 80–100<br>90 | 8–12<br>10 | 1–3<br>2 | 1500–4000<br>2500 | 8.5 | [85] |
| Water-soluble polymers | PEtOx | 8–183 | 180 | 30, 27, 25, and 23 | 200–220<br>210 | 3–7<br>4 | 1–3<br>2 | 200–400 | 3–7<br>5 | [86] |
| Hydrogel | PEtOzi | 45 ± 5 (dry)<br>89 ± 12 (wet) | 10<br>500 μm spacing | N/A | 130<br>Spinneret 150 | 2–4 | 1.5–2 | 1300–1800 | 3.3 | [87] |
| Photocurable polymers | Poly(LLA-*ε*-CL-AC) | 24.6 ± 2.7 | 20<br>100 μm | 30 | 130<br>Spinneret 145 | 7 | 3 | 420 | 4.5 | [88] |
| | Poly(*ε*-CL-AC) | ≈15–75<br>26.8 ± 1.9 | 10<br>5 in *x*/*y*<br>200 μm | 30 | 90<br>Spinneret 105 | 7 | 0.3–4<br>1 | 100–810<br>300 | 4.5 | [89] |
| Nondegradable polymers | PP | 20–105<br>16.4 ± 0.2 | 10 on top (wall)<br>5 in *x*/*y*<br>200 μm | 25 | 215<br>Collector 70–90<br>80 | 6.2 | 0.5–1.0<br>0.5 | 25–150<br>750 | 3.3 ± 0.5 | [90] |
| Electroactive polymers | PVDF | 25–50 | 5 | 26 | 190 ± 2 | 2.70 ± 0.08 | 1.5–3.0 | 1800–5000 | 4.0 ± 0.5 | [91] |
| Compounding particulates | 3 and 7 wt% HAp in PCL | 16.84 ± 2.41<br>20.46 ± 1.09 | 190 μm | 21 | 80 | 7 | 20 mL h$^{-1}$ | N/A | 10 | [47] |
| | Bioactive milk proteins in PCL | ≈50 μm | 5<br>300 μm | 25 μm diameter | 85 | 20 | 1 | 720 | | [29] |
| | 5 wt% 45S5 BG in PLA-PEG-PLA/PLA 10 wt% | 31 ± 2 | 10<br>5 in *x*/*y* | 23 | 142 | 4 | 2 | 5000 | 3.5 | [92] |
| | SrBG in PCL | ≈100 μm | ≈8–10<br>≈4–5 in *x*/*y* 1000 μm | N/A | 55 | −6 | 3.8<br>0.69<br>0.36 | N/A | 8 | [64] |
| | PEG and ROX in PCL | 3–10 | 0°–90° pattern<br>15<br>100 μm pore size | 45 | 95 | 2.3–2.6 kV | 0.015–0.03 | 600–1200 | 1.5 | [70] |

*Table 2: Different filaments with specifications from Kade, J. C., Dalton 2020*

**What is biofabrication and its relation to MEW**

The manufacturing process of complex biological substances by biofabrication often starts with raw materials such as biomaterials, matrices, molecules, and living cells. The introduction of 3D fabrication technologies has accelerated the development of this quickly changing technology. This field advances presently used procedures and tactics for wound healing. In an effort to improve recovery and regeneration in an effort to optimize the resulting shape and function, efforts to combine the best qualities of these technologies may be strengthened by the inclusion of progenitor and stem cell derivatives. A bioprinting tool could make it possible to biofabricate skin replacements in the patient itself in-situ. In an effort to replicate or at least simulate autologous tissue, complex constructions can be produced with stacked live cell types. The in situ biofabrication of skin replacements within the patient is possible with a bioprinting equipment. To replicate or at least approximate autologous tissue in an effort to restore healthy vascularized tissues, organs, and skin, complex structures can be produced using stratified live cell types. Biofabrication accelerated significantly with the development of advanced MEW devices. In Figure 6 there is an example of biofabrication of MEW synthesized PCL fibers.

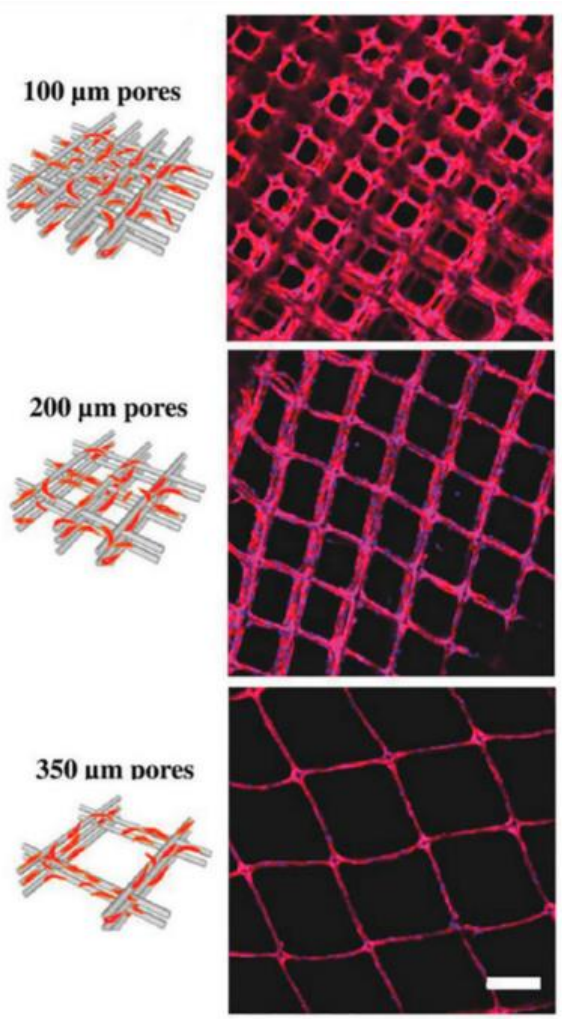


*Figure 6: Human endothelial cells attached with PCL fibers*

## Conclusion

Additive manufacturing is the way to create structures or materials affordably and fast. Most used ones are MEW and MES. These two devices act like same but main difference MES creates random fiber groups while MEW creates constant precise and detailed structures. Today, in chemistry and medicine (especially tissue engineering) uses MEW and MES to synthesize bioorganic compatible polymer structures to treatment of organs, tissues, skins etc. MEW is similar to 3D printing devices which prints plastic structures main difference is MEW precise about nanometer, micrometer sizes and can design structures with biocompatible fibers. I think in the future humanity will be design and synthesize synthetic parts for every ill-part of humans. We can already create tissues and made accelerated healing process so there is no other obstacle to getting on next level. In twenty years or so biofabrication and designing, melt electrowriting will be used in all branches of medicine.

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