

Development of Piezoelectric Polymer Substrate for Enhancing Neuronal Growth

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Abstract

Neural cells respond to myriad cues in their differentiation and migration. Electrically charged polymeric substrates featuring local voltage gradients may elicit an increase in nerve cell differentiation by producing a redistribution of local charge in response to an applied stress. Previous work has demonstrated that mouse neuroblastoma cells exhibit enhanced neurite outgrowth when seeded on piezoelectrically (PZ) active Poly(L-Lactic acid) (PLLA). Presently, a characterization study of PLLA is being conducted for the evaluation of its PZ properties as a function of its preparation, stretch ratio, and poling history. A parallel investigation will assess PLLA's effects on several cell types as a function of these same conditions.

Background

The piezoelectric (PZ) effect describes the redistribution of local charges in response to a mechanical deformation. Both dipolar domains and space charges appear to be essential components.

•Charges in PZ materials redistribute under stress or strain.

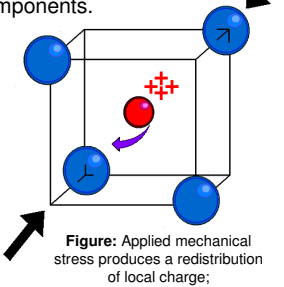


Figure: Applied mechanical stress produces a redistribution of local charge;

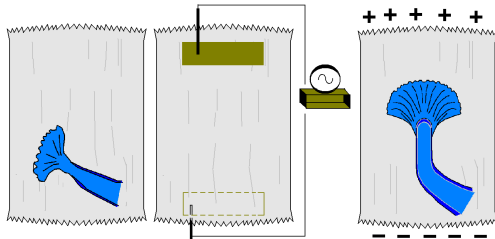


Figure: Poled PZ substrates further enhance and directionalize neurite outgrowth.

•Poly(L-lactic acid) (PLLA) is *intrinsically* PZ: becomes piezoelectrically active simply when uniaxially drawn.

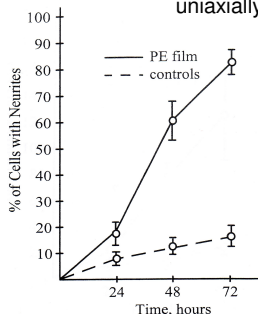


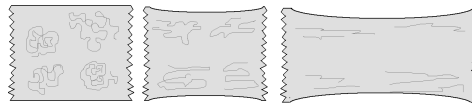
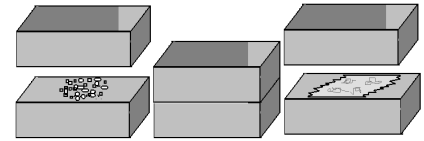
Figure: Previous lab work demonstrates enhanced neurite differentiation on PZ films.

Previous work by co-author (JIS¹) has demonstrated that mouse neuroblastoma cells exhibited enhanced neurite outgrowth when seeded on PLLA.

Methods

Melt Press

PLLA powder is melt pressed @ 210 °C, 1 minute at contact, 4 minutes 10 tons pressure, and quenched to preserve structure.



Amorphous films are drawn @ 80 °C, 10 ~.25mm/min to 2:1, 2.5:1, 3:1, & 3.5:1 to increasingly activate PZ properties.

Uniaxial Stretch

Rheograph Measurements

Elastic modulus
d,ε-constant
Dielectric Constant

Corona Poling

150 MV/m, 2mV → steps; 3 steps/min

Rheograph Measurements

Results

PLLA films drawn to 3.5:1 exhibited

- Larger elastic moduli
- Larger piezoelectric stress and strain coefficients
- 20X increase in remnant charge
- Larger dielectric constants

	Elastic Modulus (N/m ²)	d-const (pC/N)	ε-const (C/m ²)	Dielectric Constant
PLLA 2:1	2.6	0.555	0.111	1.64
PLLA 3.5:1	4.4	5.12	2.59	1.84

Table: Rheological measurements exhibit highly stretched PLLA's enhanced piezoelectric activity to that of moderately stretched PLLA.

Discussion

Piezoelectric Polymers may:

- Direct neurite outgrowth
- Be mechanically stimulated by external sources or intrinsic body vibrations

PLLA has:

- Controlled piezoelectricity
- Enhanced piezo properties when poled
- Bioresorbability
- FDA approval for implantation

Parallel work in affiliated labs (David Shreiber's Neuroengineering Research Lab):

Mechanical stimulation of the polymer films seeded with fibroblast and chick DRG cells for the characterization of cell outgrowth and optimization of stimulation conditions.

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¹Bryan DJ, Tang JB,.... Scheinbeim JI *Enhanced Peripheral Nerve Regeneration Through a Poled Bioresorbable Poly(lactic-co-glycolic acid) Guidance Channel*, Unpublished.