Synthesis of Polypeptides Using Difunctional Initiators

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Sponsor: MRL Program, NSF

Introduction

Stirring plate

Goal of Research:

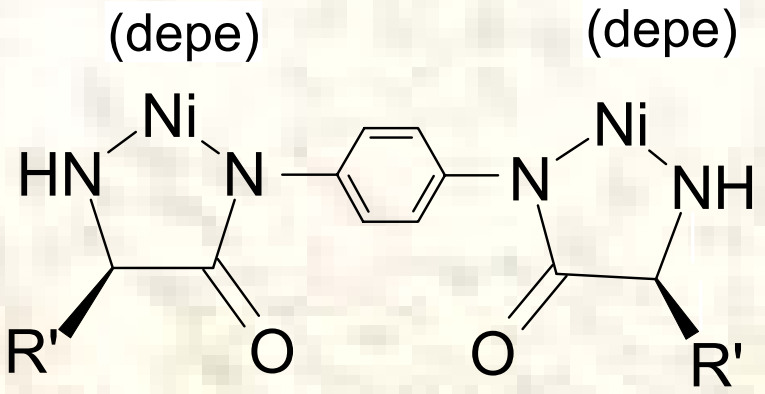
Synthesis of polypeptides using difunctional initiators.

What is an *initiator*?

It is a molecule which combines with a monomer to activate polymerization.

$$I^* + M \rightarrow I{\sim}M^* \quad \textit{(initiation)}$$

Introduction
Focus Questions



- First step: How effective are certain initiators in activating *living polymerization?*

- Next step: Are the initiators *difunctional*?

$M + {}^{*}I^{*} + M \rightarrow {}^{*}M{\sim}I{\sim}M^{*}$ *(initiation)*

$M + {}^{*}M{\sim}I{\sim}M^{*} + M \rightarrow {}^{*}M{\sim}M{\sim}I{\sim}M{\sim}M^{*}$ *(propagation)*

Methods

Experimental Objectives:

- Test and analyze effectiveness of initiators.
- Introduce "weak link" to prove difunctionality of initiators (future)

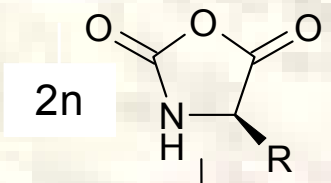
Drybox

Materials:

- 3 sample initiators
- Monomer (Glu-NCA)
- Solvents (THF, DMF, ethyl ether)

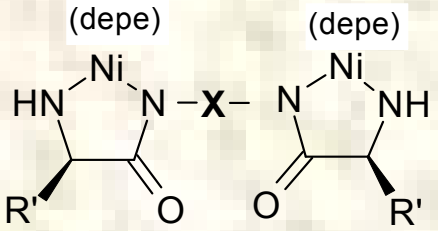
Polymerization of Glu-NCA

M + I + M* ➔ **M~I~M* (initiation)*



Init.
48 hrs
room temp
THF

CO_2

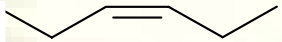
Init = 

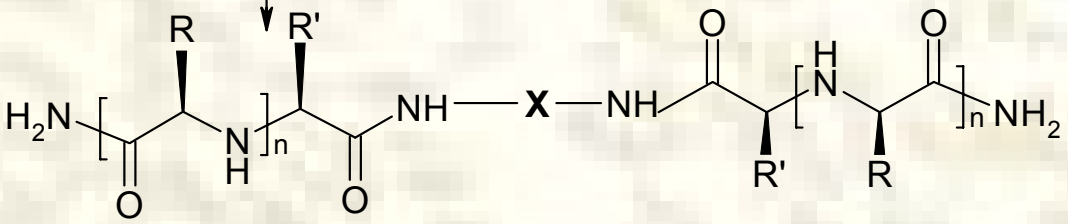
X:

Init 1 = 

Init 2 = $-(CH_2)_6-$

Init 3 = $-H_2C-C(CH_3)_2-CH_2-$

Init 4 = 



depe = 1,2-bis(diethylphosphino) ethane

R' = $-CH_2CH(CH_3)_2$

R = $-CH_2CH_2CO_2CH_2C_6H_5$

Methods

Experimental procedure

- Prepare reactants, THF solvent, and utensils.
- Polymerize Glu-NCA with initiator in drybox (oxygen & water-free). Stir 48 hours.
- Precipitate polymer in ethyl ether.
- Measure M_n & M_w/M_n using GPC.

(Repeat, varying initiator concentration.)

Synthesis of Polypeptide

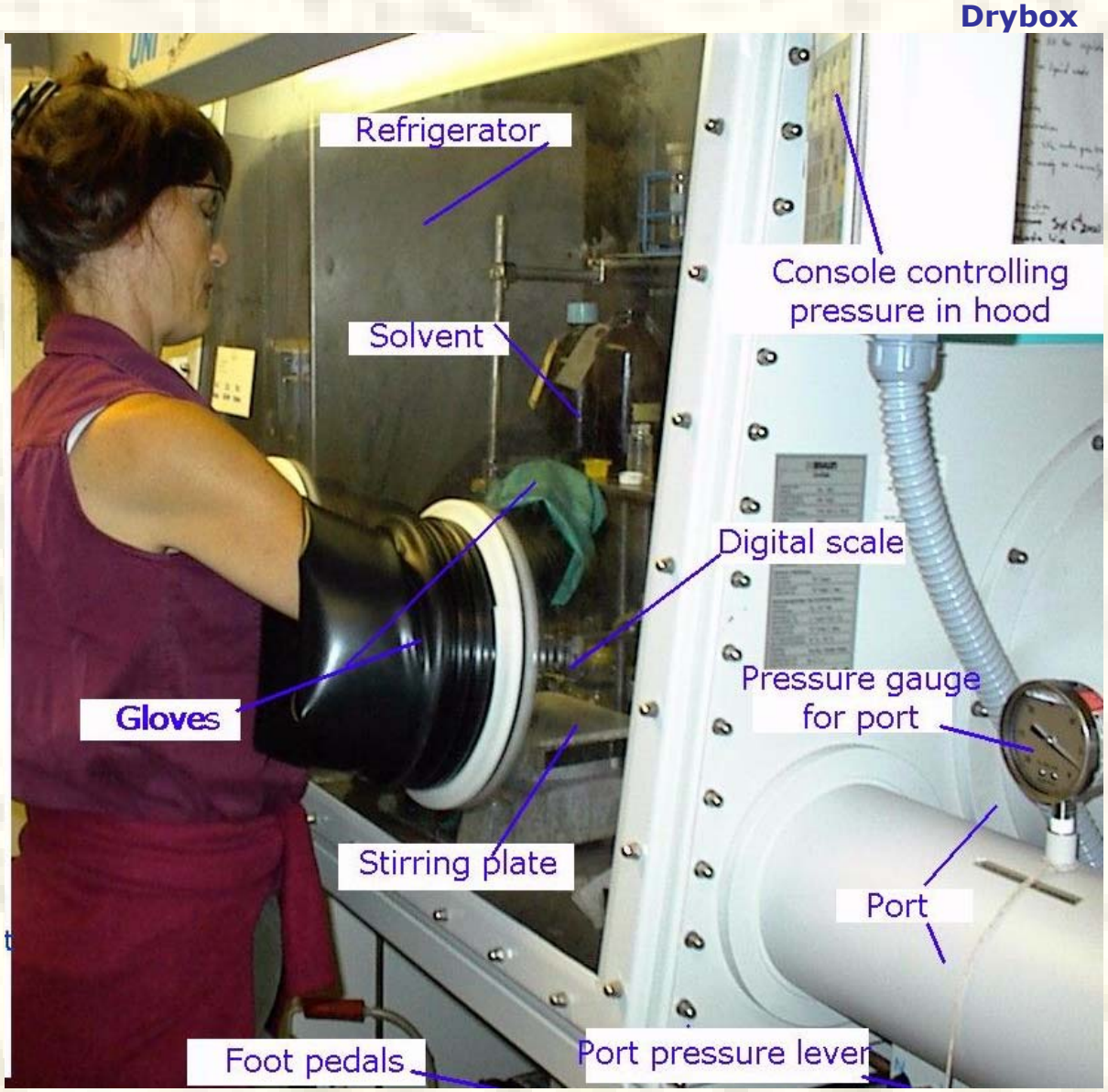
Procedure:

1. In drybox, dissolve Glu-NCA in THF. Put into reaction flask. Add initiator. Remove flask from drybox.

2. Stir at 25ºC for 48 hrs under hood.

3. Precipitate in ethyl ether and dry polymer.

4. Analyze polymer using GPC.



Analysis with GPC

1. Polypeptide is dissolved in DMF, filtered, and injected onto the columns.

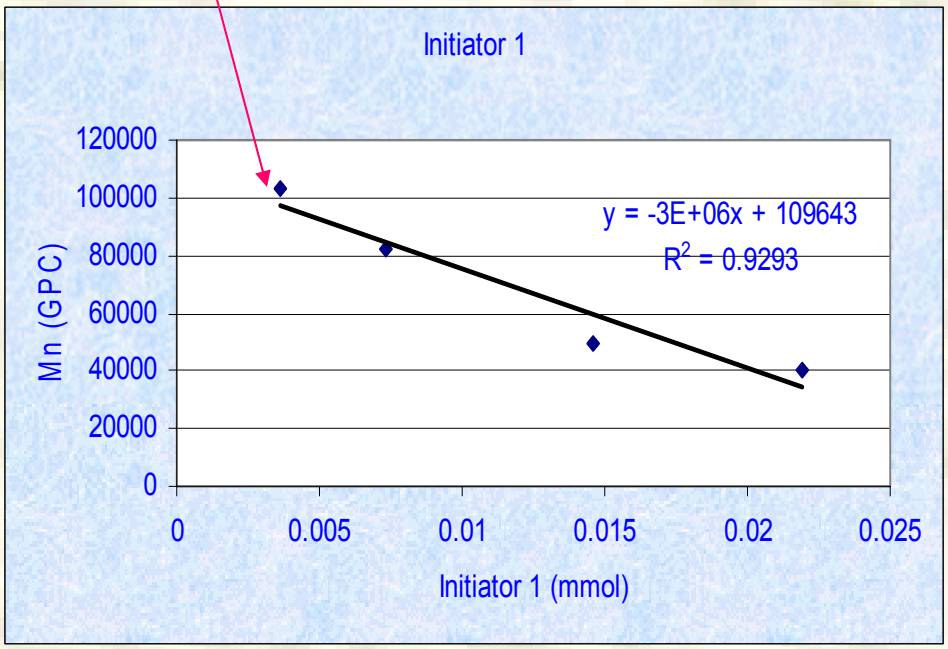
2. Large molecules move faster than smaller ones on the columns.

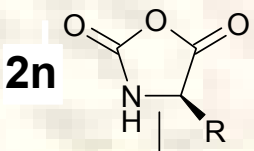
3. Polymer solution moves from columns to light scattering and RI detectors. Large molecules arrive and are detected by laser first, then smaller ones.

4. Detector sends data to computer program, which plots curve and prints report.

Results

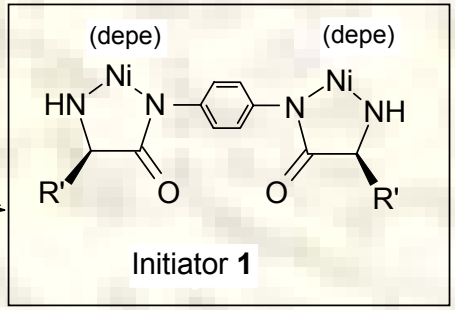
I (mmol)	M_n (GPC)	PDI (M_w/M_n)
0.00365	317500	1.2



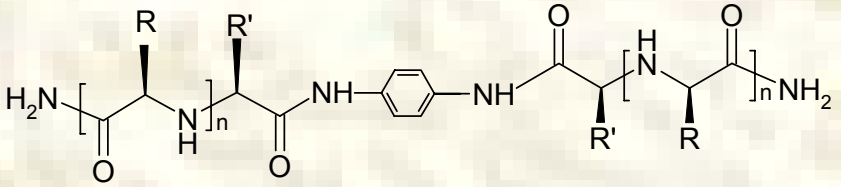


CO_2

Init.
48 hrs
room temp
THF

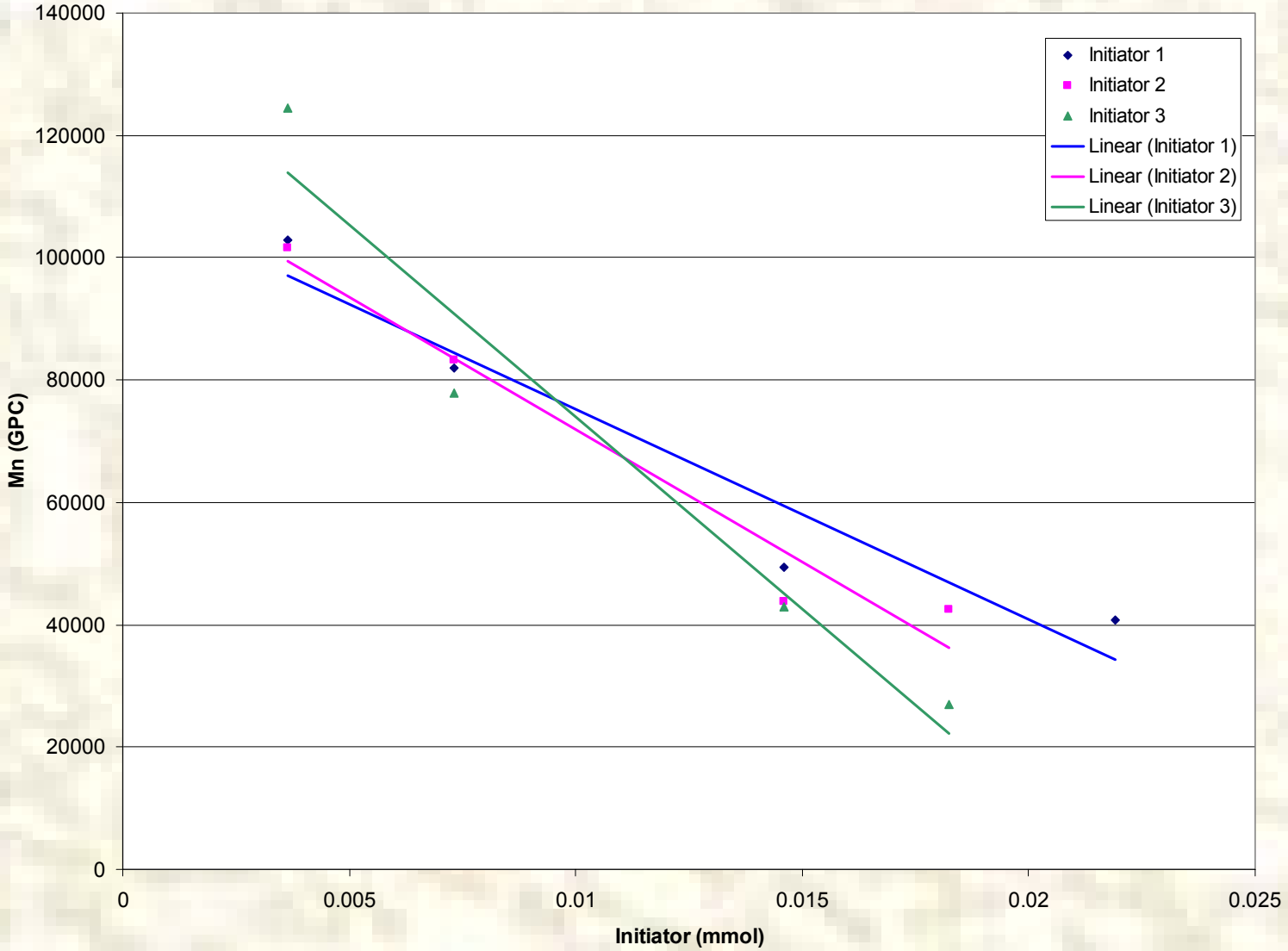


Initiator **1**



Results

M_n vs Amount of Initiator

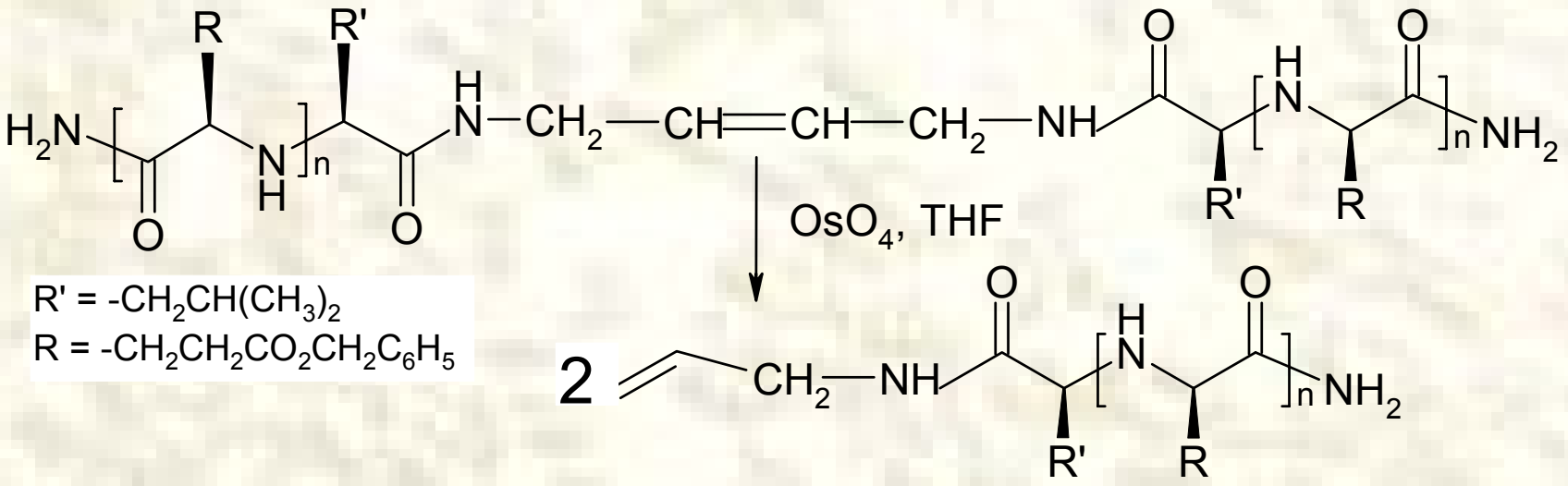


Conclusions

Despite different core structures, all initiators effectively polymerized Glu-NCA.

Future work

Prove difunctionality of initiator:



R' = $-CH_2CH(CH_3)_2$

R = $-CH_2CH_2CO_2CH_2C_6H_5$

If initiator is difunctional: *by GPC* ➔ $M'_n = 1/2\ M_n$

Potential application

- Use difunctional initiators to prepare ABA block copolymers.

  A~A~B~B~I~B~B~A~A

- Create polypeptides with predetermined properties and sizes.

Fume hood

Personal Reflections

- Scientific research is an inquiry-based and data-driven process of discovery. *The questions and answers are not provided beforehand.*

- Scientists are persevering. *Formal research is a long-term, sometimes tedious, carefully documented process.*

- Formal research integrates other academic disciplines. *i.e. statistics, technology, communication, & literacy.*