PATENT ASSIGNMENT

Electronic Version v1.1
Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT

CONVEYING PARTY DATA

Name	Execution Date
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Molly S. Shoichet	02/11/2004

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PROPERTY NUMBERS Total: 1

Property Type	Number
Application Number:	11988207

CH $40.00 11988207

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Total Attachments: 6
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University of Toronto

OFFICE OF THE VICE-PRESIDENT, RESEARCH AND ASSOCIATE PROVOST

ASSIGNMENT OF RIGHTS TO THE UNIVERSITY OF TORONTO BY THE INVENTOR

In consideration of the sum of two dollars ($2.00) and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, **Yumin Yuan, M olly S. Shoichet, and** their heirs, executors, administrators and assigns (collectively the "**Assignor**") hereby sell, assign and transfer to The Governing Council of the University of Toronto, its successors and assigns (collectively the "**Assignee**") all right, title and interest which the Assignor now has or may hereaftcr have in an invention described as

Novel Diene (Dienophile) Functionalized Biodegradable Polymers and Novel Method of Surface Biomodification by Diels-Alder Chemistry

in Appendix A annexed hereto, (the "Invention")

including, without limitation, the right to apply for patents in Canada, the United States of America and any other country, the right to receive any letters patent that may be issued from any such applications, the right to have any letters patent that have been granted transferred into the name of the Assignee, and the right to sell, license or assign the Invention or the rights thereto.

The Assignor hereby releases the Assignee from any and all manner of claims and demands which the Assignor may now have or may in future have in respect of the Invention or in connection with the patenting, sale or licensing thereof.

Executed at Toronto, Ontario this 11th day of February, 2004.

Witness

Inventor(s)

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Appendix A

UNIVERSITY OF TORONTO INVENTIONS POLICY
CONFIDENTIAL INTELLECTUAL PROPERTY DISCLOSURE

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1. **Title:**

Novel Diene (Dienophile) Functionalized Biodegradable Polymers and Novel Method of Surface Biomodification by Diels-Alder Chemistry

2. **a) University of Toronto Inventors/Major Contributors:**

SURNAME, GIVEN NAMES	UNIVERSITY PERSONNEL NO.	DEPARTMENT (LIST ANY CROSS APPOINTMENTS OR AFFILIATED INSTITUTIONS)	AFFILIATION WITH UNIVERSITY (i.e. faculty, res. assoc., post-doc, student, staff, visitor, etc.)	CURRENT ADDRESS, PHONE, FAX, EMAIL
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2. **b) External Inventors/Major Contributors:**
(Please provide names and affiliations of non-University of Toronto individuals who have made a creative contribution to this Intellectual Property, i.e. sponsor employees, academic collaborators, etc.)

none

3. **Description:**
(Please highlight the novelty or patentable aspects of this Intellectual Property; attach a separate sheet if necessary)

We have invented a new series of functionalized, biodegradable homopolymers and copolymers consisting of a new monomer repeat unit alone and of co-monomers. The novel repeat unit in homopolymer and copolymer structures has diene (or dienephile) functional group. The titled

DATE RECEIVED: NOV 24 2003 DISCLOSURE REFERENCE NO.: RIS 1087
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homopolymers and copolymers were synthesized either directly from polymerization of monomers or from derivatization of polymer precursors, resulting in diene- or dienephile-derivatized polymers such as poly(trimethylene carbonate) (PTMC), polylactide (PLA), poly(lactide-co-glycolide) (PLGA) and polycaprolactone (PCL), which are well known for biodegradability and biocompatibility.

In this invention, novel biodegradable polymers containing a diene or a dieneophile group were synthesized by the following three methods: (1) Aminolysis or alcoholysis of biodegradable polymers (in bulk or on surface); (2) Modification of biodegradable polymers by diene (or dienophile) through reactive functional groups such as COOH, NH_2, allyl, OH, epoxy, HS etc. or through their derivatives in bulk or on surface; (3) Direct polymer synthesis from a diene (or dieneophile monomer) by ring-open polymerization in solution or in bulk, or by solution polycondensation. Typical dienes include furan and its derivatives, butadiene and its derivatives, cyclopentadiene and its derivatives; typical dieneophiles include maleimide and its derivatives, maleic anhydride and its derivatives.

Example 1: Polymer surface (bulk) functionalization through aminolysis and alcoholysis

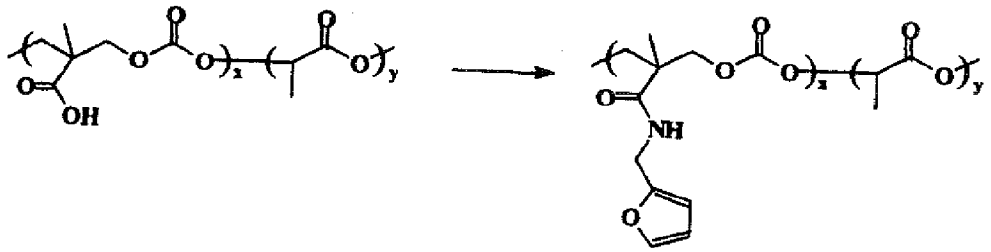
A biodegradable aliphatic polyester such as PLA, PLGA, PCL and PTMC was dissolved in THF, furfuryl amine or furfuryl alcohol (diene) was added and the mixture was refluxed for a period of time. After cooling down, the polymer was recovered by precipitation into non-solvent.

Example 2: Polymer modification

A biodegradable polymer bearing functional groups were synthesized. The functional groups include, but do not limit to COOH, NH2, allyl and OH, were reacted with furfuryl derivatives, resulting furfuryl functionalized copolymers.

Case1:

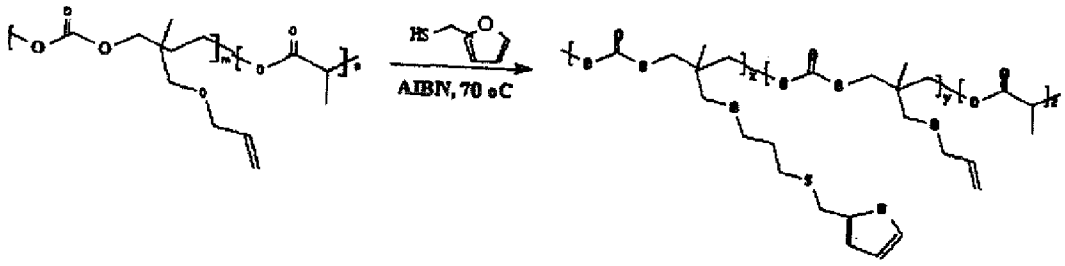
A biodegradable copolymer bearing COOH group was dissolved in anhydrous THF, 1.2 molar equivalent CDI was added. After stirring for about 30 minutes, 1.5 molar equivalent furfurylamine was added and stirred for an additional 1 h. The copolymer with furfuryl group was recovered by precipitation in water and dried in a vacuum oven.



Scheme 1

Case 2:

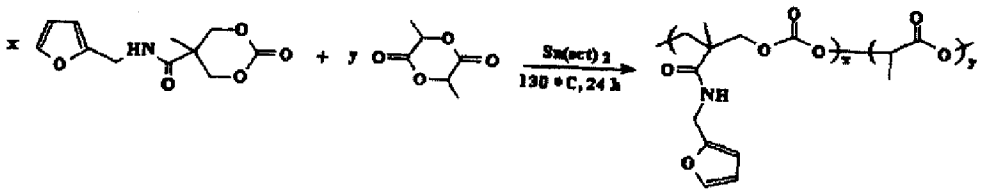
An allyl functionalized copolymer was dissolved in toluene together with 0.2 equivalent of AIBN (based on allyl content). After 3 cycles of freeze-thaw, the vial was heated at 70 °C for 24 h. The copolymer was recovered by precipitation in non-solvent. About 25 ~ 40 mol % of allyl group was substituted by furfuryl group, revealed by 1H NMR analysis.



Scheme 2

Example 3: Copolymerization

Furfuryl-derivatized trimethylene carbonate was copolymerized with d,l-lactide by bulk ring open copolymerization at 140 °C for 24 h.



Scheme 3

We also invented a new method of surface biomodification of biodegradable polymers based on our invented diene and dienophile polymers through interfacial Diels-Alder reaction, as shown in the Figure 1. This is a simple, one-step reaction that preferably occurs in aqueous solutions and requires neither catalysts nor coupling agents. Furthermore, there are no byproducts of this reaction. The specific chemistry is described below.

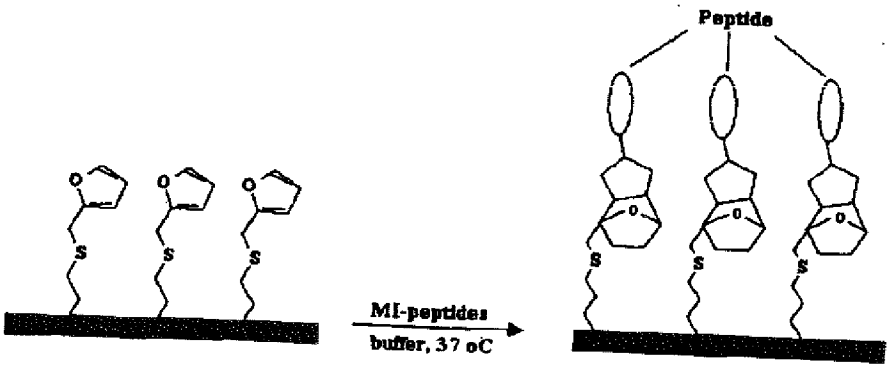


Figure 1. Surface modification by Diels-Alder reaction

The diene (or dienophile) functional group on the biodegradable polymer surface can undergo interfacial (or surface) Diels-Alder reaction with dienephile (or diene) functionalized molecules in aqueous solutions, typically the biomolecules, such as peptides, proteins and drugs. After interfacial Diels-Alder reaction at ambient temperature, the molecules, typically the biomolecules such as peptides, proteins and dugs, can be covalently immobilized onto diene (or dienophile) functionalized biodegradable polymer surfaces which imparts the biodegradable polymer the bioactivity. Thus, a novel method of peptide surface immobilization is established. The advantages of this method are: (1) Reaction conducted in aqueous solution and ambient temperature; (2) No additives required and no side reactions or products produced; (3) High reaction efficiency; (4) Extendable to immobilize peptides onto 3 dimensional scaffold surface. This kind of bioactive material has potential applications such as drug delivery carrier, implants and scaffolds.

Example 4. A biodegradable polymer containing furfuryl (a diene) functional group (from Example 3, Case 2) can react with a maleimide (a dieneophile) functionalized oligopeptide containing YIGSR and RGD sequences in aqueous buffer solution at ambient temperature (room temperature to 37 °C). After certain times (1 ~ 24 hours), the surface becomes increasingly hydrophilic (water contact angles of 30°/10°) comparing to the controls (water contact angles of ~80/60). Oligopeptide was covalently immobilized onto the polymer surface through cycloadduct by Diels-Alder reaction. Primary chick DRG neurons respond remarkably by extending neuritis on these peptide-modified surfaces.

4. **How was the work leading to this Intellectual Property funded?** I.e. salaries, equipment used, supplies etc.

SPONSOR	GRANT OR CONTRACT FUND #	INTELLECTUAL PROPERTY TERMS & CONDITIONS
NSERC, PREA	451750, 415773	none

5. **Where did the work leading to this Intellectual Property take place?**

Mining Building, Room 322

6. **Is this Intellectual Property subject to any software licence, material transfer, confidentiality, non-disclosure, collaboration or other agreement, written or oral, not referenced in Section 4?**
___x___**NO** _____**YES** (If "Yes", please provide details)

7. **What are the potential applications and/or sources of revenue from this Intellectual Property?**

Tissue engineering, drug delivery

8. **Warranty:**

I/We, the Inventors/Contributors listed in Section 2(a), have read, understood and agree to all of the preceding and declare that all of the information provided in this disclosure is complete and correct. To the best of our knowledge, all persons who might legally make an ownership claim in this Intellectual Property are identified in Section 2(a) and 2(b).

Yumin Yuan Nov. 19. 2003
Signature Date
Typed Name: Yumin Yuan

Molly Shoichet 11/19/03
Signature Date
Typed Name: Molly Shoichet

Signature Date
Typed Name:

Signature Date
Typed Name:

For more information on University of Toronto Intellectual property policies, please call 416-978-7833 or access http://www.library.utoronto.ca/techtran/.
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