both sustained release of the bioactive component as well as a template for infiltration of new cells and tissue.

**[0013]** Scaffolds synthesized from two-component polyurethanes have been shown to degrade to non-cytotoxic decomposition products and to support the ingrowth of cells and new tissue in vitro and in vivo. By varying the composition, scaffolds with tunable mechanical properties ranging from soft elastomers to leathery and glassy plastics have been prepared. Additionally, biodegradable polyurethane scaffolds prepared from linear segmented elastomers were shown to support controlled release of bFGF, suggesting the potential utility of polyurethane scaffolds for drug delivery applications.

**[0014]** Embodiments of the present invention include novel methods of incorporating a bioactive element, such as an antibiotic into a reactive polyurethane (PUR) scaffold. The effects of scaffold hydrophilicity and degradation rate on tobramycin release and bioactivity were investigated, as well as the effects of tobramycin on the dynamic mechanical properties of the polyurethane scaffolds.

**[0015]** Another embodiment of the present invention is a method of delivering a bioactive agent to a wound site, including a bone fracture site, using injectable, biodegradable polyurethane foams. These materials support osteoblast cell migration and proliferation, and degrade to non-cytotoxic decomposition products. Polyurethane (PUR) scaffolds have also been shown to promote ingrowth of new cancellous bone when implanted in the iliac crest of sheep.

**[0016]** Embodiments of the present invention include PUR scaffolds to release antibiotics using at least two approaches: (1) incorporation as a powder, and (2) microencapsulation in PLGA microspheres. These biomaterials present potential clinical opportunities for treatment of various indications, including osteomyelitis.

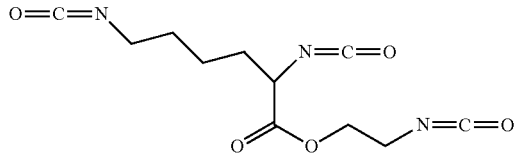
**[0017]** Aspects of the present invention relate to methods and compositions for treatment of bone fractures. Specific embodiments of the present invention include products, and methods related to materials are injectable, biodegradable, and undergo controlled degradation and release of bioactive components. Scaffold degradation and release of bioactive components can be controlled independently. Conventional materials, such as tricalcium phosphates, polymethyl methacrylate, and poly(D,L-lactide-co-glycolide) cannot meet all of these performance requirements.

**[0018]** Scaffolds of the present invention may be both biodegradable and resorbable, so it can minimize total surgery time and invasiveness for patients. Furthermore, PMMA bone cement only delivers approximately 2-5% of its encapsulated tobramycin, while scaffolds of the present invention have a 50-90% delivery efficiency rate. A great benefit of the reactive liquid molding synthesis of our scaffolds is that it allows them to be injectable and therefore minimally invasive during implantation. In addition, they can expand to fill the contours of the fracture site, enhancing bone-scaffold contact and fixation.

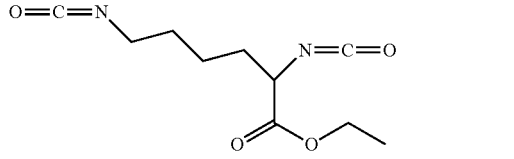
**[0019]** Embodiments of the present invention offer injectable polyurethane scaffolds incorporating tobramycin were prepared by reactive liquid molding. Scaffolds had compressive moduli of 15-115 kPa and porosities ranging from 85-93%. Tobramycin release was characterized by a 45-95% burst (tuned by the addition of PEG), followed by up to 2 weeks of sustained release, with total release 4-5 times greater than equivalent volumes of PMMA beads. Released tobramycin remained biologically active against *S. aureus*, as verified by Kirby-Bauer and time-kill assays. Similar results were observed for the antibiotics colistin and tigecycline. The versatility of the present invention, as well as their potential for injection and controlled release, may present promising opportunities for new therapies for healing of infected wounds.

**[0020]** Thus, embodiments of the present invention include biodegradable polyurethane scaffolds that comprise at least one polyisocyante, polyisocyanate prepolymer, or both; at least one polyester polyol; and at least one catalyst. The density of said scaffold is from about 50 to about 250 kg m-3 and the porosity of the scaffold is greater than about 70 (vol %) and at least 50% of the pores are interconnected with another pore; and the scaffold incorporates at least one biologically active component in powder form. The biologically active component may have a hydroxyl or amine group. Additionally, the biologically active component may be at least one antibiotic, protein, anti-cancer agent, or combinations thereof. Examples include at least one of tobramycin, colistin, tigecycline, BSA, PDGF, BMP-2. In embodiments of the invention, the biologically active component is in powder, including a labile powder.

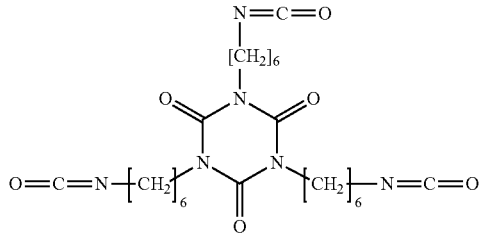
**[0021]** In other embodiments of the present invention, the polyisocyante is an aliphatic polyisocyanate. Examples include lysine methyl ester diisocyanate (LDI), lysine triisocyanate (LTI), 1,4-diisocyanatobutane (BDI), and hexamethylene diisocyanate (HDI), and dimers and trimers of HDI.




LTI




LDI




Desmodur N3300A
(HDI trimer)

**[0022]** In embodiments of the present invention the biologically active agent is present in an amount of from about 2 to about 10 wt %; or the biologically active agent is present in an amount of from 4 to about 10 wt %. When the biologically active agent is an antibiotic, it may be present in an amount, for example, of from about 1-12 wt %. As another example, when the biologically active agent is a protein, it may be present in an amount of from about 0.01 to about 10000 μg/ml