INTRODUCTION:
The goal of tissue engineering is to develop a replacement biomaterial or constructs to restore the structure and function of damaged or degenerated tissue. The paradigms of tissue engineering are based on some combination of a) cells, b) growth factors, and c) substrates that are combined into an implantable tissue replacement. Mechanically induced tissue formation could be considered the fourth paradigm. Mechanical aspects like the frequency and magnitude of appropriate mechanical cues remain elusive; yet arguments that tissue is accentuated under biomechanical culture can scarcely be refuted [1,2].

The goal of this study was to investigate to what extent bio-mimetic optimization of synthetic scaffold micro-architectures could improve tissue formation under load-bearing applications. Improved de-novo tissue growth may result in accelerated scaffold integration, reduced risk of secondary complications and scaffold failure, and better clinical outcome. Since such experiments are highly variable when conducted in a laboratory setting, we opted for a numerical approach as a first step. Computer models eliminate biological variability and allow the direct investigation of multiple independent parameters.

METHODS:
In this study, the micro-architecture of unit building blocks for scaffolds was manipulated through bio-mimetic optimization of scaffold/implant topologies. The scaffold topology is essentially material independent with the goal to promote uniformity of the surface mechanical environment during loading. Simulation of de-novo tissue growth on the optimized scaffold micro-architecture elaborates on the benefit of the proposed method.

The methodology was split into three different parts:
1) Determine the mechanical parameter most likely to stimulate bone formation under loading
2) Use a bio-mimetic approach to manipulate a scaffold’s surface mechanical environment
3) Determine tissue growth based on scaffold optimization method

RESULTS:
Analysis of the tissue surface mechanical environment at unconfined compression provided the most accurate representation of trabecular bone’s static constraints. Von Mises stress was the most non-uniform of the mechanical parameters, while strain-energy density was the most uniform parameter.

For the bio-mimetically optimized scaffold (Figure 3), more surface areas shared a common strain-energy density value, thereby fostering a more distributed pattern of tissue growth. The result is a narrowing of the scaffold’s mechanical distribution and a shifting of the mean value to a higher strain energy state. Consequently, fewer tissue elements were resorbed and more tissue elements were added, producing a more uniform tissue pattern on the scaffold surface.

DISCUSSION:
Tissue replacement scaffolds need to follow design features that are based on the final product, 100% de-novo tissue. To achieve that goal, the micro-architectural features of the scaffold need to address several challenges. One of these challenges is the smooth transition from synthetic polymer to natural tissue while maintaining functional load bearing. Another challenge is the uniformity of de-novo tissue growth, which may prevent regional scaffold collapse during degradation.

Our bio-mimetic scaffold micro-architecture optimization approach yielded two hundred percent more tissue growth with a superior tissue pattern compared to the non-optimized scaffold. The advantage of our technique to other previously published tissue adaptation schemes [5] is that the architecture optimization was performed at the tissue surface level.

Although our approach increases the complexity of the scaffold micro-architecture, various direct printing techniques are close to fabricate similar scaffolds to scale and the needed size. There are, however, several limitations to our approach that will have to be addressed in future studies. Experimental studies will have to verify the findings and show clearly differences in uniformity between various mechanical parameters.

REFERENCES:

ACKNOWLEDGEMENT:
NSF-ITR DMI-0427216