Porous Scaffolds for Bone Tissue Engineering

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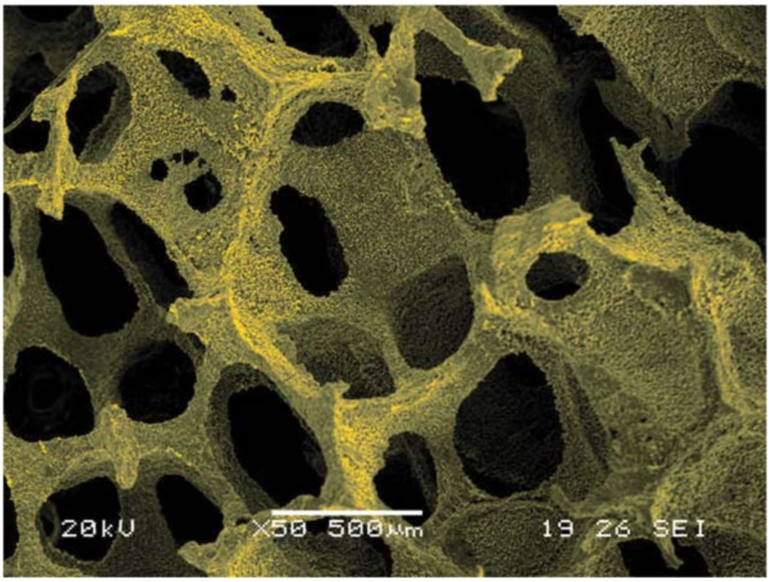


Contents

Summary

The Synthesizer tool in CES EduPack, combined with materials information in the Bioengineering database provides new possibilities to explore and select materials for medical implants. In this case study, we investigate hybrid materials for scaffolds in bone tissue engineering. The implants are modeled as bioceramic foams with a range of porosity. The resulting materials can be compared to human tissue and biomaterials in property charts which helps the understanding and design of suitable scaffolds.

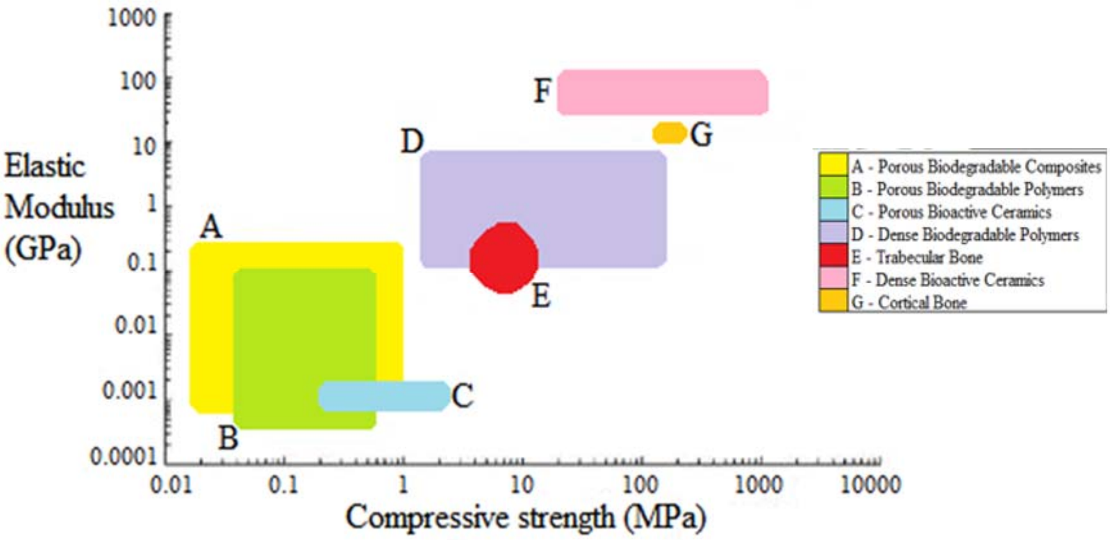
Due to the complex biological environment that biomedical materials are subjected to—particularly implanted devices—it is time consuming, costly and difficult to test a large range of potential candidates. This makes accurate data and the synthesizer approach to estimating new or combined material properties very useful.

1. What is the scope?

Bioengineering is a broad and cross-disciplinary area ranging from biomaterials to tissue engineering. One essential aspect of materials with biological function is, of course, biocompatibility. However, compatibility of physical and mechanical properties can also be important. This is the case for implants that are part of the skeletal system.

In the field of bone tissue engineering, bioactive glass-ceramic scaffolds have generated significant interest, as they can provide a 3D template that promotes new bone formation. Such scaffolds have proven that they can mimic trabecular bone structure as well as exhibit adequate mechanical properties and bioactivity to support the growth of new bone tissue [1].

Biomechanical properties of bone implants are critical to their structural function *in vivo*. They should be approved for use in the human body, naturally, but must also have appropriate porosity to be assimilated by the body. The porosity of the implant material is linked to its average (effective) density in a linear fashion; the more porous, the lower the implant density. It is also linked to other properties, such as strength or stiffness.



Comparison of mechanical properties for a variety of biomaterials including polymers and bone [2]

Our objective in this case study is to explore the use of the Synthesizer tool in CES EduPack to investigate the influence of porosity on the biomechanical properties of a hybrid scaffold material (foam). We also want to compare these properties with other relevant biomaterials and biological materials. The starting point will be bone-like materials, such as calcium phosphates and bioglasses, that fulfill typical biomedical constraints. The main mechanical property to consider is the compressive strength.

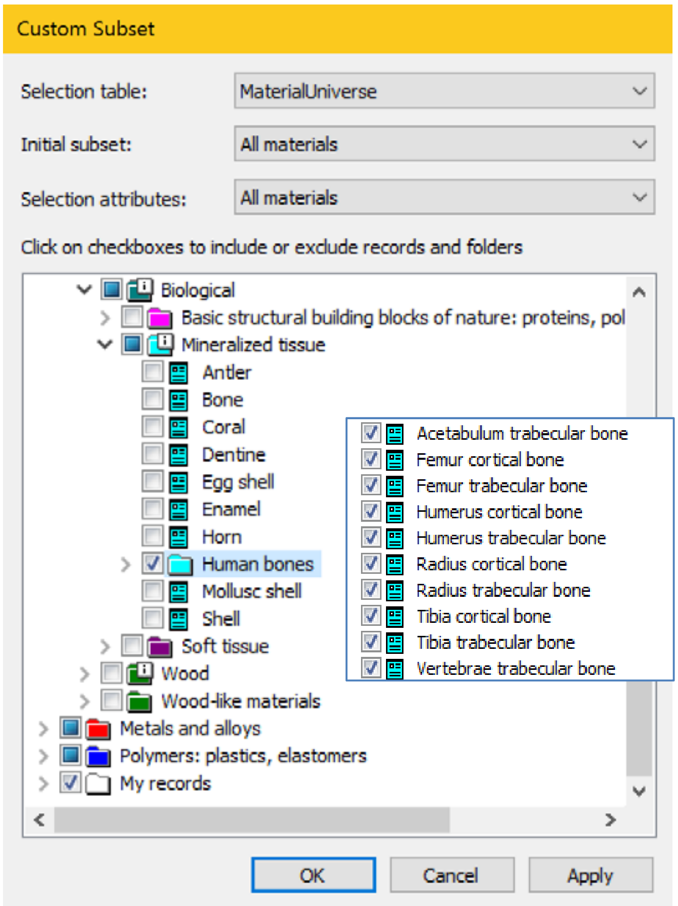
The man-made scaffolds have a porous structure that mimics the trabecular bone porosity. They have the ability to induce the formation of hydroxyapatite (HA) on their surfaces in physiological conditions that naturally encourages bone attachment and promotes bone regeneration. However, these scaffolds exhibit certain drawbacks in terms of their mechanical performance, as they do not have the required compressive strength for safe handling and for load-bearing applications. Moreover, these materials have not yet been fully tailored to enhance their bone-regeneration capabilities. Nor has the structural integrity of the scaffolds been optimised, including their resistance to crack propagation (work of fracture).

2. How to tackle the problem

CES EduPack can provide a systematic approach for material selection, *i.e.,* screening and subsequent ranking based on material performance indices. This can easily be applied also to biomedical materials, since this is one of several provided subsets within the Bioengineering Edition. However, in this case study, the objective is different.

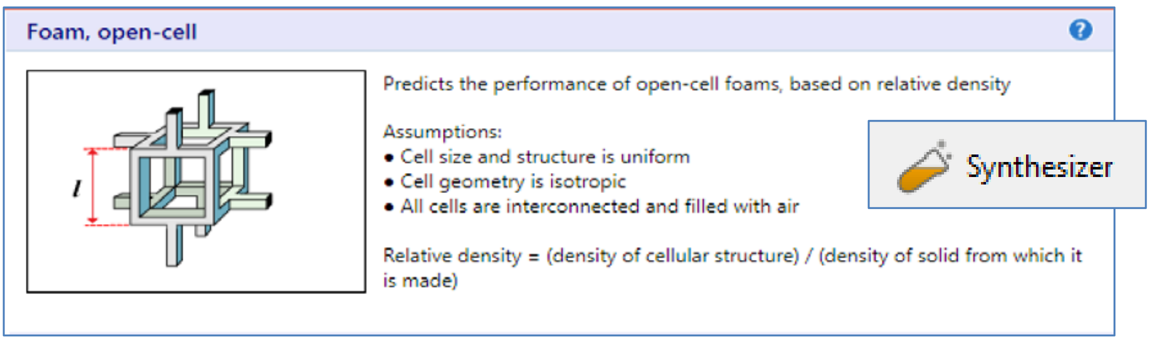
We want to compare existing biological and biomedical materials with a range of hybrid materials, with properties estimated by the models of the Synthesizer tool. This tool is now available in the Bioengineering Edition of CES EduPack, allowing bench-marking of the simulated hybrids with relevant reference biomaterials, such as PEEK, titanium and HA.

The platform for this comparison is the *Bioengineering Level 3* database of CES EduPack, containing data records for over 4000 materials. We can quickly limit the number of reference materials by creating a custom subset of biological materials and selected polymer, ceramic and metal biomaterials, as indicated to the right.

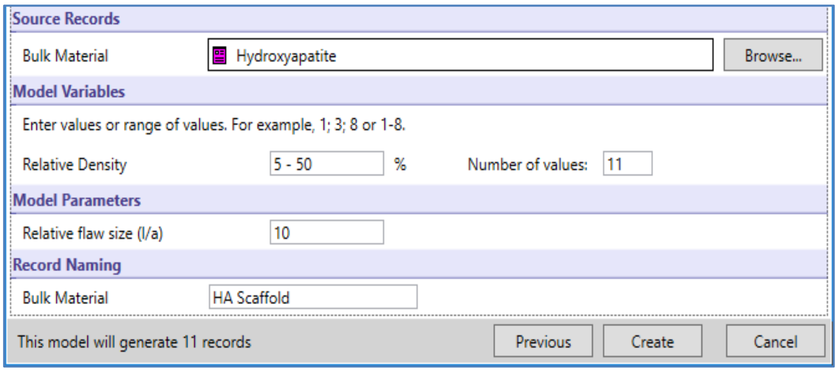


3. Using CES EduPack to synthesize hybrids

After compiling a suitable subset for comparisons, we can choose a model from within the Synthesizer tool. Porous ceramics can be represented by *open-cell foams*. In this case study, the aim is to explore a real-world research problem of creating a scaffold that mimics the properties of bone.



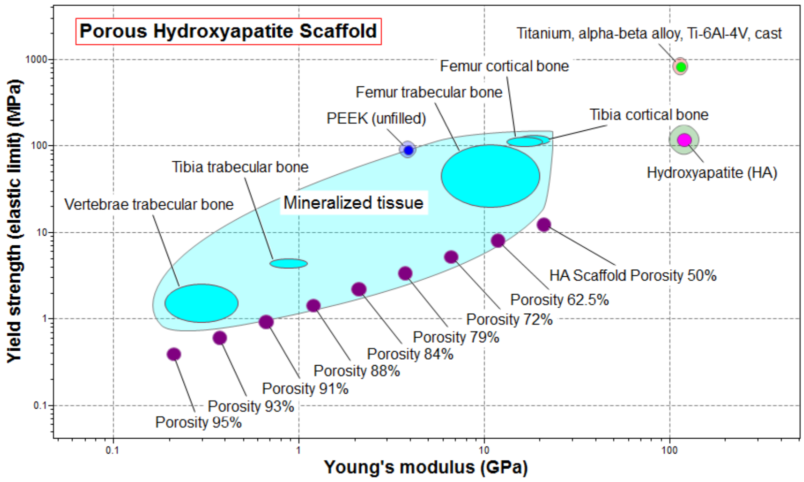
Starting with typical mechanical properties, *Yield strength* and *Young's modulus*, we can create data records from the synthesis of HA foam with a *relative density* ranging from 5 to 50%. The relative density for a foam is defined as the effective density of the cellular hybrid divided by the density of the solid material it is made from. The relative density values in our chart corresponds to a *porosity* between 50 and 95%.



The example below corresponds to a foam generated by the open-cell synthesizer model. The chart is based on the input shown to the left. The number of values generated and the range of relative densities can be adapted, depending on the needs. The range of this foam is chosen to cover the stiffness range of mineralized bone tissue and the l/a value is left as the default (10).

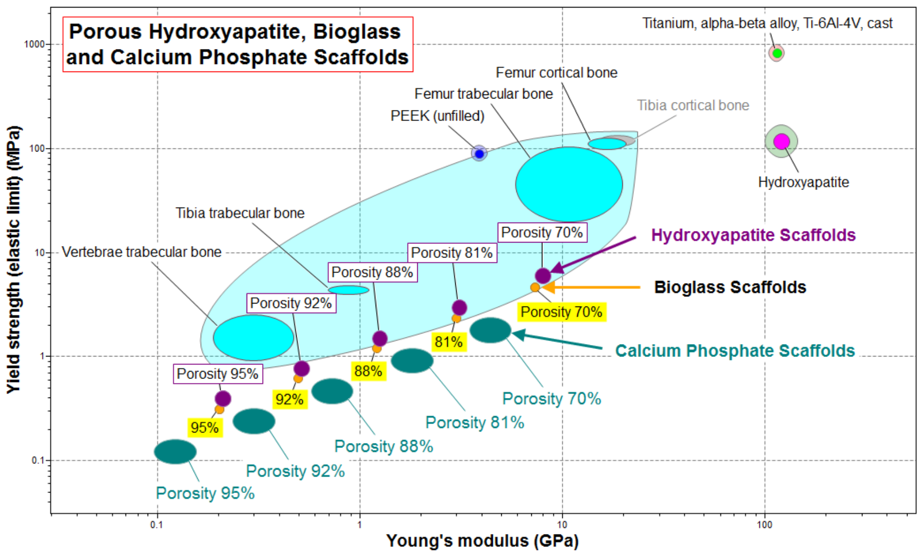
In order to create the new data records, it is necessary to give them a name in the dialogue box. In this case, 11 new records are created in a folder with the generic name *My records*. These can then be plotted, labelled and re-colored (by right-clicking) to appear as desired in the chart.

Chart showing mechanical properties of synthesized hybrids together with selected reference materials



4. Results

Focusing on the main issue of how the compressive strength depends on porosity, we can plot three scaffold materials in a chart of these reference materials, as shown below. Interestingly, all three sets of modeled materials show compressional strength comparable to those of trabecular bone but falling short of those needed to mimic cortical bone. This means that these scaffolds couldn't be used for load-bearing applications. Considering the requirements of a minimum porosity, at least 70% is needed to allow cells, waste, and other essential substances to flow through the scaffold to aid in bone regeneration.

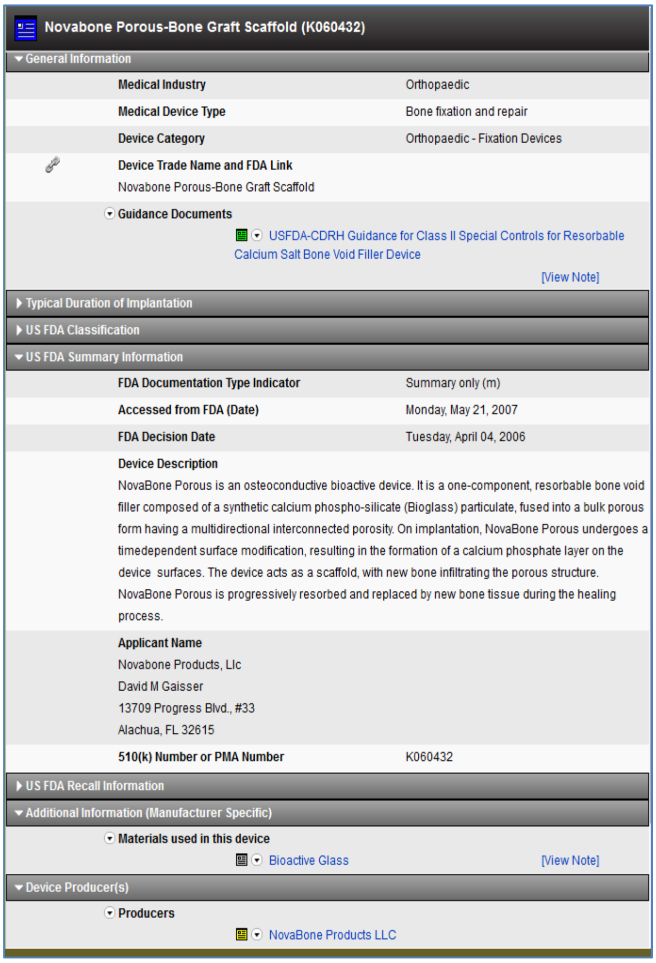


The estimated properties of the highly porous Bioglass, Calcium Phosphate and Hydroxyapatite scaffolds with their counterpart bulk materials as well as trabecular and cortical bone data for comparison

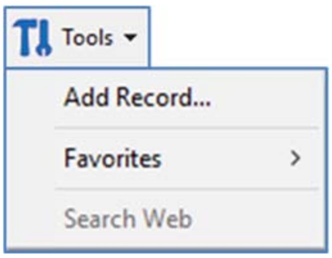
5. Analysis and reality check

Bone tissue scaffolds is a fast-emerging application area, as the demand for transplantable tissue currently outstrips supply. This is one of the main driving forces behind the development of this type of implant. There is a great deal of research going on to improve the current crop of scaffolds through creating composites or coating scaffolds with biodegradable polymers to strike a balance between the mechanical properties needed to support the bone regrowth and other functional requirements.

Due to the deficiency in compressional strength, there are currently not a vast number of these highly porous scaffolds on the market and the ones that are tend to be used in non-load-bearing situations. One such example is the Novabone Porous-Bone Graft Scaffold produced from Bioglass by Novabone Products LLC. More information about the range of scaffolds on the market can be found in the ASM Medical Materials Database (adjacent) that is accessible via the Bioengineering Edition of CES EduPack with the appropriate subscription.



We have shown that the Synthesizer tool allows the comparison of simulated materials with data from the database. You can, however, also add other external porous materials data from research straight into the chart. In the bar-chart below, we have added a number of examples from referenced sources (see Table). These are added using the *Add Record* feature available in the Tools menu (or by right-clicking directly in the chart). These additional reference materials are shown as dark blue bars in the resulting chart.

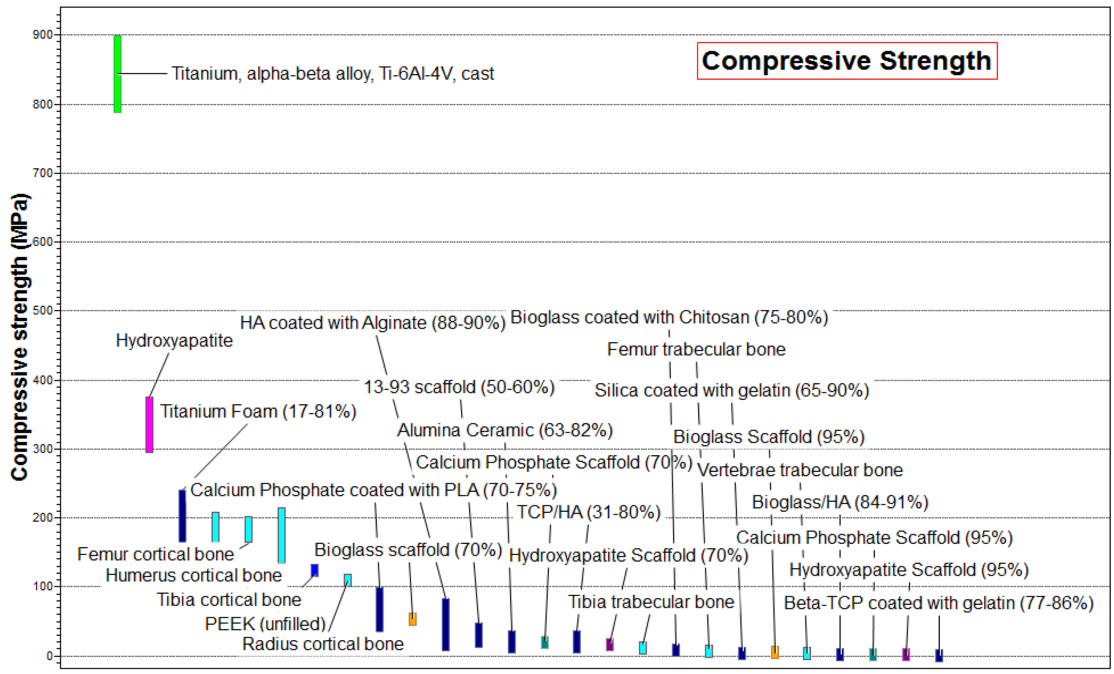


Up to 10 additional records can be added into your project via the Tools menu, and saved with your chart in a Project file

Table of additional reference material from research papers

Material name	Porosity range (%)	Compressional Strength range (MPa)	References
Bioceramic 13-93	50 - 60	10 - 47	[3, 4]
Alumina Ceramic	63 - 82	2.6 - 37	[5]
Titanium Foam	17 - 81	150 - 240	[6-8]
TCP/HA	31 - 80	2 - 36	[9-11]
Bioglass/HA	84 - 91	0.87 - 2.78	[12]
Silica coated with Gelatin	65 - 90	0.24 - 8	[13]
Hydroxyapatite with Alginate	88 - 90	6.3 - 83	[14]
Bioglass coated with Chitosan	75 - 80	1.2 - 15	[15]
Calcium Phosphate coated with PLA	70 - 75	28 - 99	[16]
Beta-TCP coated with Gelatin	77 - 86	0.11 - 0.78	[17]

The materials found in research papers span a range of mechanical properties, as can be seen below. Notably, titanium foams show that there are cellular materials that combine compressive strength, comparable with cortical bone, with a high degree of porosity. Whereas pure titanium alloys may be too stiff and hard for mechanical compatibility, the foams offer possibilities to moderate these properties while providing channels for body fluids and integration. The issue of biodegradability, however, remains a problem.



A final bar-chart showing the critical property for bone tissue implants with added research data [3-17]

6. What does CES EduPack bring to the understanding?

CES EduPack produces highly visual results which, combined with the expertise of an educator, can help to teach bioengineering in an engaging and interactive way. It aids exploration and promotes good materials decisions in many relevant areas.

In this case study, CES EduPack suggest the following conclusions:

- The Bioengineering database has a large number of relevant specialized materials and data organized into useful subsets, as demonstrated for biomedical materials.
- The Synthesizer tool can be used to model mechanical properties of highly porous materials so they can be matched with, for example, trabecular bone.
- Bulk materials used currently in bone tissue engineering, such as Hydroxyapatite, calcium phosphate and Bioglass ceramics can be used as reference materials. These can easily be compared with simulated porous materials and can be utilized as benchmark for improvements.
- When comparing the highly porous materials with the bone it is trying to mimic, the mechanical properties do not yet compare to those of cortical bone. With the addition of coatings or a change in composition, the mechanical properties of the scaffolds could match those of bone, as demonstrated by titanium foam.

The Bioengineering database of the MaterialUniverse provides generic material property data, enabling main material properties to be compared to estimates generated in the Synthesizer tool. The next step may be to use a specialized database, such as the ASM Biomedical Materials Database, available via CES EduPack for those who have a subscription with ASM. These give more detailed information about specific scaffolds and bulk materials which can be explored as a more advanced extension to this case study.

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