Hard Tissues, Biomineralization, and Our Health
Key points...

Bio...
- How could some biomolecules be able to “engineer” some very tough materials such as hard tissues?
- Implications in human health

Physics...
- Structure synergy
- Biomineralization
- Demineralization
Hard Tissues ~ Biominerals

The backbone of life

Mastication, proper speech, weapons of attack/defense,…

Pearl

Skeleton, support, protect, mineral reservoir, …
Implications: regenerate hard issue

The abalone shell is a microlaminate structure of CaCO$_3$ crystals and protein, with a fracture-toughen 3,000 times greater than that of the individual crystal alone.
Some more examples

Calcium carbonate: CaCO₃

Calcite

Aragonite

Vaterite

Amorphous
Think about it…

- Why do hard tissues have such superior properties?
- Here we need to look at …
  - the correlation between the inter-particle structure and the designated properties.
Implications

Lesson from Nature

- To regenerate hard tissues and treat some disease, such as dental caries, osteoporosis, etc.
- **One day**... we may be able to fabricate some high performance materials (ultra hard and elastic) in terms of nanostructure engineering/architecture.
Structural synergy

- In hard tissues, the synergy of “needles” or “plates” gives rise to the unusual properties of these “materials”.
- Structural synergy: *crack stopper*
- Biomineralization
- Organisms form minerals
  - contrast with abiotic mineralization

- calcite
The hardness of hard tissues will increase with the ordering of “plates” or “needles”.
Structural synergy: crack stopper

- Stopping the cracks…

Mosaic structure
Structural synergy: crack stopper

- Stopping the cracks...
Structural synergy: how does nature do it?

Biomineralization!!
- Nucleation on cell as substrate
- Common ion: Ca^+
Nucleation outside the cell
● Nucleation between cells
Nucleation inside a cell

assembly

exit

exit

exit

no exit

Growth unit

assembly

mineral

organic matrix as substrate for accumulation and continued growth of unit

active pumping

passive diffusion

secretion
Implications: regenerate hard issue

To repair the damage caused by dental caries requires more than $10 billion annually in the USA

Look ma, no fillings
What if dentists could regenerate a broken tooth?

**Tooth: Synergistic packing of HAP crystallites and mechanical properties**

Ca$_5$(PO$_4$)$_3$OH (Hydroxyapatite-HAP)

Small angle X-ray scattering
Tooth: Synergistic packing of HAP crystallites and mechanical properties

- $\phi$: an ordering parameter to show the alignment of needle crystals:
  - $\phi = 100\%$ complete alignment.
  - $\phi = 0\%$ complete misalignment.
- The hardness of the dental sample increases drastically with the ordering.
What is the difference between living bone and a pillar of plaster?

- A pillar of plaster can't repair any cracks and eventually it crumbles away.
- The living bone is continuously repairing itself -remodeling.
Structural synergy: *Ordered structure of bone*

**Microstructure, nanostructure**

Cross section of bone

- **Rings of protein and salts**
- **Blood vessels**
- **Bone cell**

Ca$_5$(PO$_4$)$_3$OH (Hydroxyl apatite-HAP)

33% organic matrix, 67% HAP

Thickness of calcium-phosphate platelets: 2-4 nm
Terminology

- There are three special types of cells that are found only in the bone. These cell names all start with "OSTEO" because that is the Greek word for bone.
Way inside the bone: through the microscope

- While looking at the bone under the microscope, measurements can be made using a computer.
Way inside the bone: through the microscope

33% organic matrix, 67% HAP

Two-thirds: phosphorus, calcium --- rings

Rest collagen

Columns withstand stress
Way inside the bone: through the microscope: *Bone Structure*

- The bones in the skeleton are not all solid.
- The outside **cortical bone** is solid bone with only a few small canals.
- The inside of the bone contains **trabecular bone** which is like scaffolding or a honey-comb.
Way inside the bone: through the microscope:

**Bone Structure (cont’d)**

To observe the mineralized portion of bone:
- The bone is green (dyes are used to make calcium green).

This is the section after it has been stained.
Way inside the bone: through the microscope

- Cortical bone
  - Cross section
  - Longitudinal section
Way inside the bone: through the microscope: *Bone Structure*

Do you know...

- Bone is the important organ to make blood and some fat cells: The spaces in the bone are filled with fluid bone marrow cells, which make the blood, and some fat cells.
**Way inside the bone: through the microscope: The O’ Cells (cont’d)**

**OSTEOCLASTS** are large cells that dissolve the bone, make canals, cavities.

- they come from the bone marrow and are related to white blood cells.

- they consist of two or more cells that fuse together, so the osteoclasts usually have more than one nucleus.

Red spots - osteoclasts. Here they are in a circle.
Way inside the bone: through the microscope: *The O' Cells (cont’d)*

- **OSTEOBLASTS** are the cells that form **new** bone:
  - coming from the bone marrow and are related to structural cells;
  - Having only one nucleus.
- **Osteoid**: protein secreted by osteoblasts, made of bone collagen and other proteins:
  - found on the surface of the new bone;
  - controlling calcium and mineral deposition.

The thin cells (hard to see) right next to the osteoid are called **OSTEOBLASTS**.
Way inside the bone: through the microscope: *The O’ Cells (cont’d)*

Osteoblasts → new bone
→ secrete osteoid = collagen → mineralizes
→ calcium phosphate deposited

osteoblasts become trapped/called osteocytes (osteo = bone, cyte = cell).

... eating away

See them here at work!

... line up on surface, increase its size
Way inside the bone: through the microscope: *The O' Cells* (cont’d)

1) osteoclasts resorb bone; 2) osteoblasts form bone.

At border between them
- resorption ends and bone formation begins:
- cement line (1 to 5 microns):
Way inside the bone: through the microscope: *The O' Cells (cont’d)*

- **OSTEOCYTES** are cells inside the bone:
  - Predecessors of osteocytes are osteoblasts. Some of the osteoblasts turn into osteocytes while the new bone is being formed, and the osteocytes then get surrounded by new bone.

- These cells can sense pressures or cracks in the bone and help to direct where osteoclasts will dissolve the bone.

The little black dots in the middle of the green bone are called **OSTEOCYTES**.
Living bone

- The movie shows what happens in one place. You'll see a little crack, then cells will turn into osteoclasts and dissolve (resorb) the bone, then cells from the marrow space will turn into osteoblasts and build new bone.
The movie shows this process on a larger section of bone where at least ten places are getting remodelled.
The living bone is continuously repairing itself. This repair process is called "Bone Remodeling". Whenever there is a tiny crack inside the bones, for example, after landing from a high jump, the bone cells will dissolve the area around the crack and fill it in with new bone. At any one time this is happening in millions of places throughout the skeleton.

... BUT ... what happens after a sever fracture?
Living bone (cont’d)

bone forming at a fracture

collagen fibers are randomly organized, very loosely packed -- results from the rapid manner in which bone is laid down.
What happens when bone remodelling goes awry?

- Estrogen is a hormone that becomes low during menopause in older women.
- Without estrogen, the osteoclasts become more active and dissolve more bone.
- Even when some minor fractures appear in the bone, sometimes the osteoclasts will dissolve right through a piece of bone.
OSTEOPOROSIS

- This bone is from a 65-year old woman. This shows that the osteoclasts have dissolved a tunnel right through a piece of bone.
OSTEOPOROSIS

- A particularly serious kind of osteoporosis is seen in people who take a medicine called prednisone. Some children have to take this medicine, too. It makes the osteoclasts dissolve more bone and the osteoblasts don't work well. Patients have lots of broken bones, especially in the back.
A summary of the O’s cells

OSTEOCYTES: to sense pressures or cracks in the bone and help to direct where osteoclasts will dissolve the bone.

- OSTEOCLASTS: to dissolve the bone.
- OSTEOBLASTS: to form new bone.
- Osteoid: bone collagen (protein) and other proteins controlling calcium and mineral deposition
Key points

- The superior properties of hard tissues are attributed to the structural synergy of biominerals and proteins.
- Bone remodeling and related diseases.
Main references

- Oral Histology: Development, Structure, and Function