Calcium phosphate mineralization occurs in both extra- and intrafibrillar spaces of collagen (left and right images, respectively). Engineers at Washington University in St. Louis experimentally proved how the confined collagen structure contributes to reducing thermodynamic energy barrier to intrafibrillar nucleation for bone mineralization. Credit: Washington University in St. Louis

Most of us don't think about our teeth and bones until one aches or breaks. A team of engineers at Washington University in St. Louis looked deep within collagen fibers to see how the body forms new bone and teeth, seeking insights into faster bone healing and new biomaterials.

Young-Shin Jun, professor of energy, environmental & chemical
engineering in the School of Engineering & Applied Science and
director of the Environmental NanoChemistry Lab, leads a team of
experts in nucleation, the initial step in forming a solid phase in a fluid
system.

While nucleation of minerals in bone and teeth is not well understood,
researchers do know that bone minerals form inside of collagen, the
main protein found in skin and other connective tissues. Jun and Doyoon
Kim, a doctoral student in her lab, studied how miniscule gaps in
collagen's fiber structure facilitate the nucleation of calcium phosphate,
which is necessary for bone formation and maintenance.

The findings, recently published in *Nature Communications*, provide a
new view into the current theory of calcium phosphate nucleation in a
confined space.

To observe nucleation in a collagen gap—about 2 nanometers high and
40 nanometers wide—the team studied calcium phosphate nucleation
with in situ small-angle X-ray scattering at the Advanced Photon Source
in Argonne National Lab. They found that without an inhibitor,
nucleation initially took place outside of the collagen gap. When they
added an inhibitor, the process occurred mainly within the collagen gap.
Jun said the extremely confined space in the collagen gap allows calcium
phosphate to form only along the length of the gap and minimizes
surface interactions with the gap sidewalls. In other words, the
topography of the collagen gap decreases the energy cost and enables
nucleation.

"When we understand how new bone forms, we can modulate where it
should form," Jun said. "Previously, we thought that collagen fibrils
could serve as passive templates, however, this study confirmed that
collagen fibrils play an active role in biomineralization by controlling
nucleation pathways and energy barriers. If we can tweak the chemistry
and send signals to form bone minerals faster or stronger, that would be helpful to the medical field."

While this study focused on the biological aspects of nucleation, Jun said an advanced understanding of nucleation in confinement also applies to chemical engineering, materials science and environmental science and engineering.

"Confined space is a somewhat exotic space that we have not explored much, and we are always thinking about new material formation without any limitation of space," Jun said. "However, there are so many confined spaces, such as pores in geomedia in subsurface environments or in water filtration membranes, where calcium carbonate or calcium sulfate form as scale. This paper is a snapshot of one health aspect, but the new knowledge can be applied broadly to energy systems and water systems."


 Provided by Washington University in St. Louis