Title: Studying protein adsorption on bone surfaces using molecular simulations

Date: Dec 05, 2013 04:05 PM

URL: http://pirsa.org/13120026

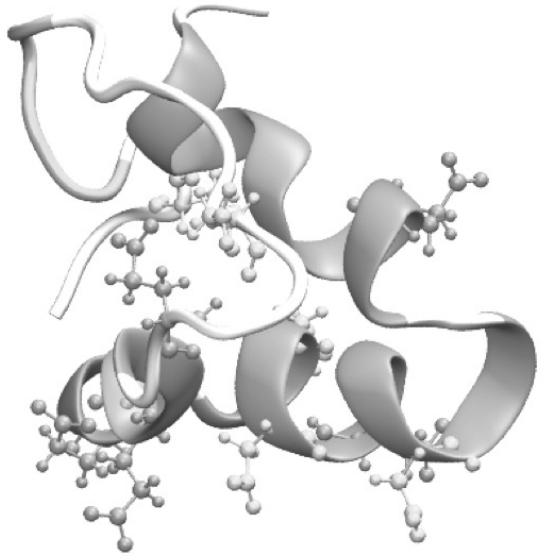
Abstract: Mineral-associated proteins have been proposed to play a central role not only in assisting the growth of biomineral crystals in hard tissues but also in preventing or limiting mineral formation in soft tissues. The elucidation of protein-biomineral interactions may lead to the design of mineralized tissues with novel properties and most importantly the development of therapies for common diseases such as kidney stones calcification in blood vessels osteoporosis etc. However the mechanism of the interaction at this unique organic-inorganic interface is still poorly understood. X-ray crystallography techniques have provided important information on the adsorbed states. Unfortunately these methods have limitations in determining the driving forces of the adsorption and the underlying roles played by the lattice ions and ionic solutions. We employ all-atom enhanced-sampling simulations and free-energy calculation techniques to characterize these interactions with the final goal of designing proteins with improved adsorption properties and capacity to prevent or enhance crystal growth.

Protein Adsorption on Bone Surfaces

Waterloo Soft Matter Conference Dec 5,

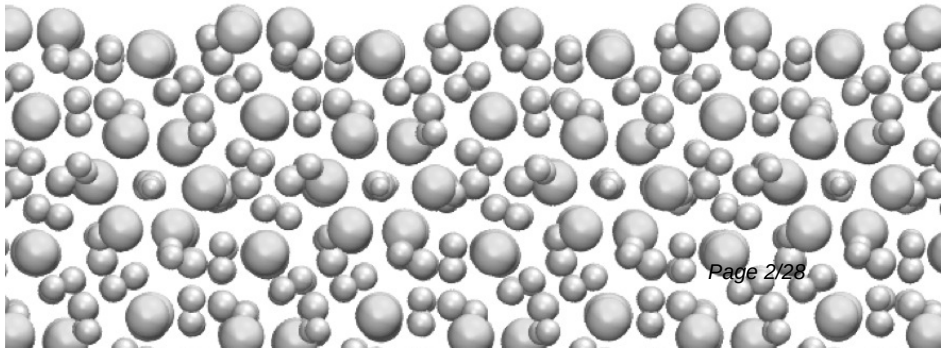
Trang Do

University of Waterloo



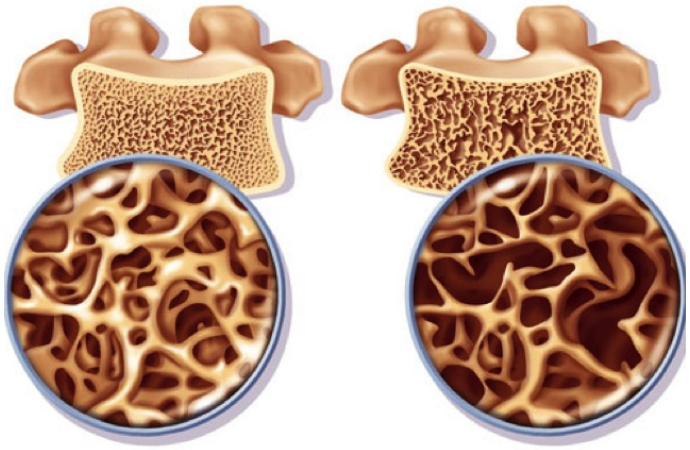
Matthew Hoopes, Mikko Karttunen
University of Waterloo

Harvey Goldberg, Graeme Hunter
Western University



Biomineralization-related diseases

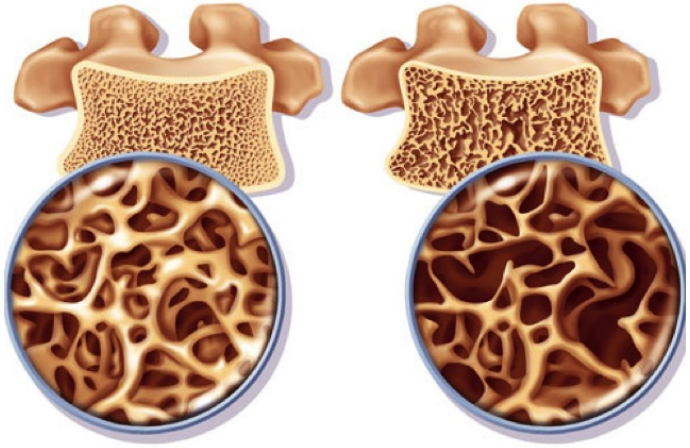
Hard tissues



normal bone osteoporosis

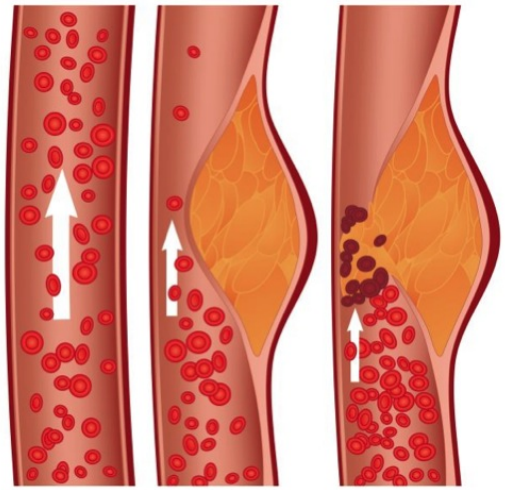
Biomineralization-related diseases

Hard tissues

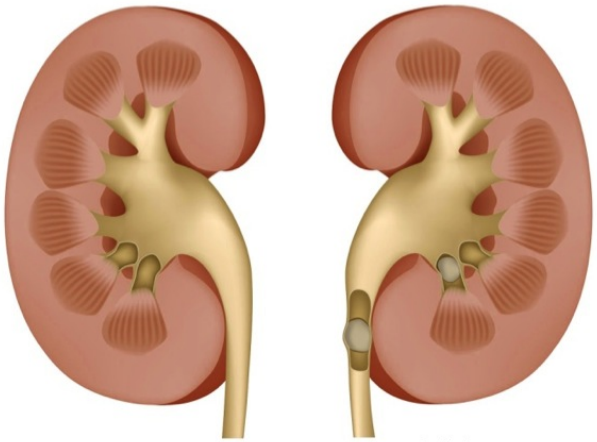


normal bone osteoporosis

Soft tissues



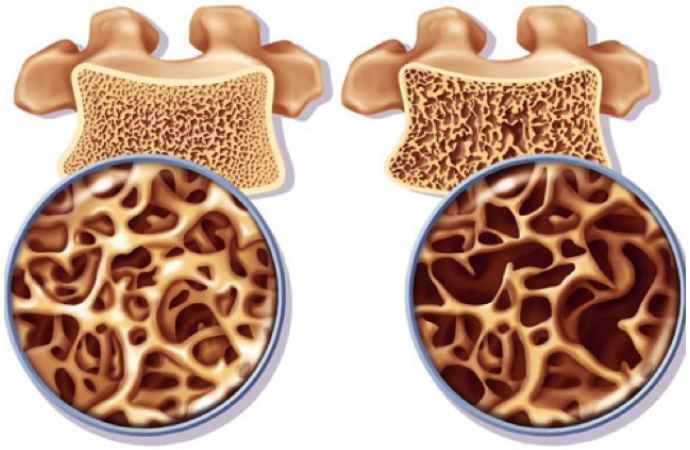
normal blood vessel atherosclerotic plaque



normal kidney kidney stones

Biomineralization-related diseases

Hard tissues

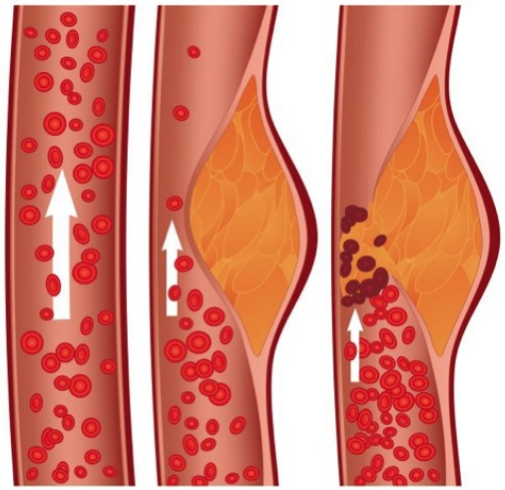


normal bone osteoporosis

Hydroxyapatite (HA) surface

$Ca_5(PO_4)_3(OH)$

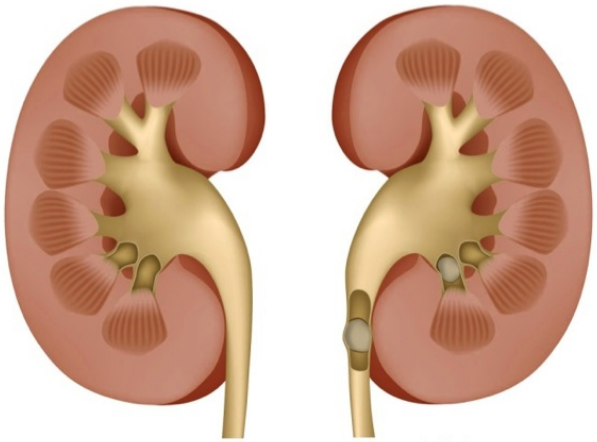
Soft tissues



normal blood vessel atherosclerotic plaque

Calcium Oxalate Monohydrate (COM) surface

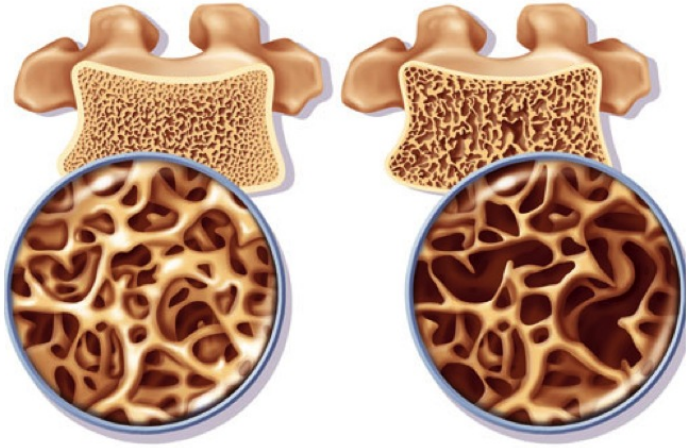
CaC_2O_4



normal kidney kidney stones

Biomineralization-related diseases

Hard tissues

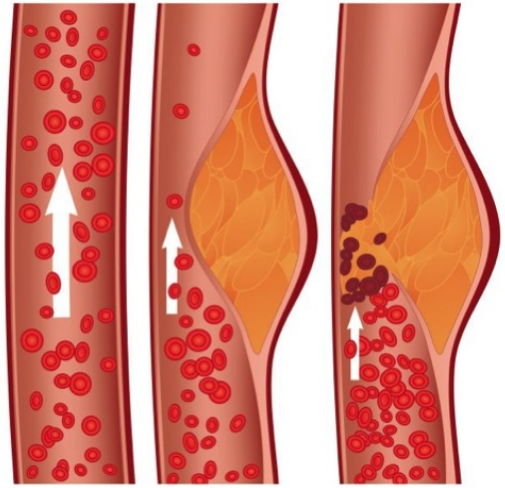


normal bone osteoporosis

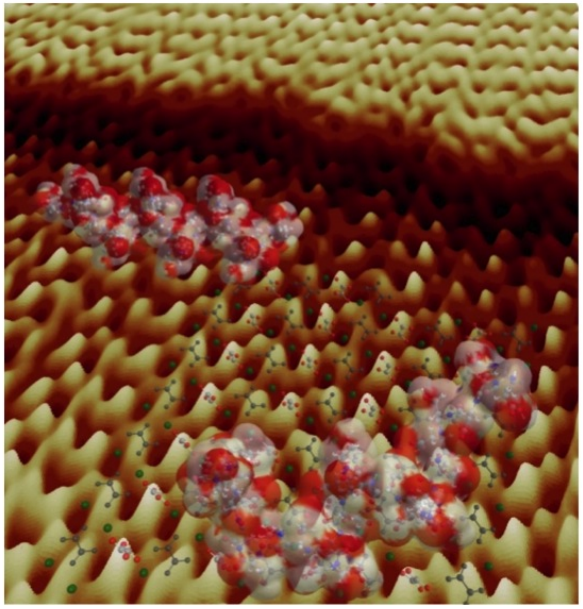
Hydroxyapatite (HA) surface

$Ca_5(PO_4)_3(OH)$

Soft tissues



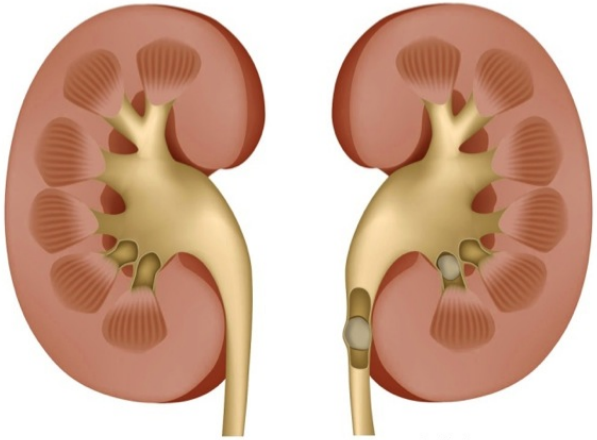
normal blood vessel atherosclerotic plaque



protein adsorption on a COM surface

Calcium Oxalate Monohydrate (COM) surface

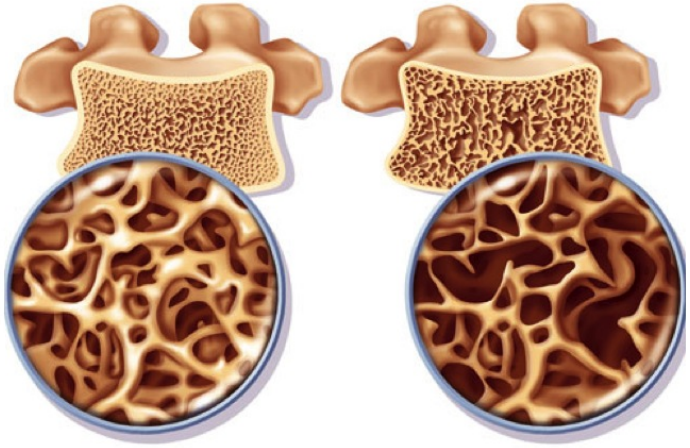
CaC_2O_4



normal kidney kidney stones

Biomineralization-related diseases

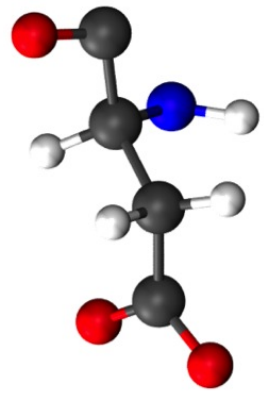
Hard tissues



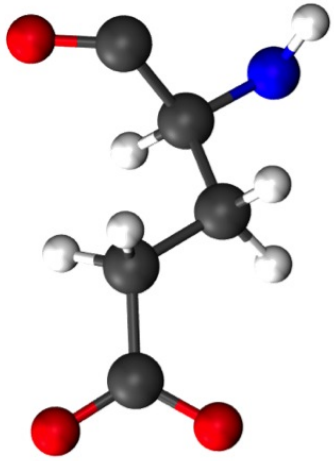
normal bone osteoporosis

Hydroxyapatite (HA) surface

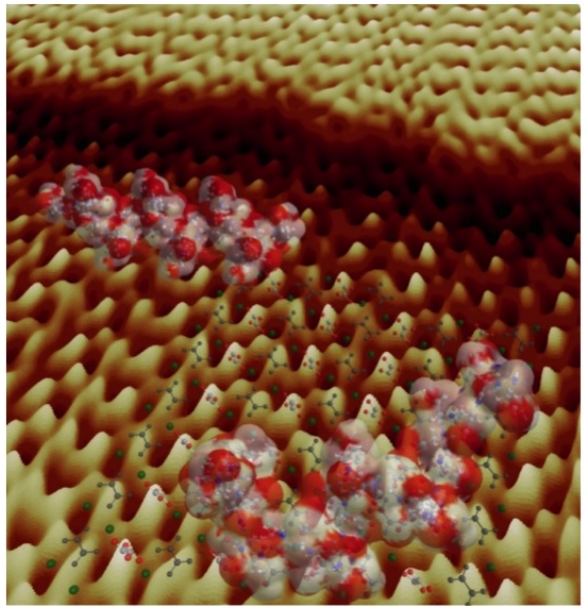
$Ca_5(PO_4)_3(OH)$



Aspartic acid (ASP)



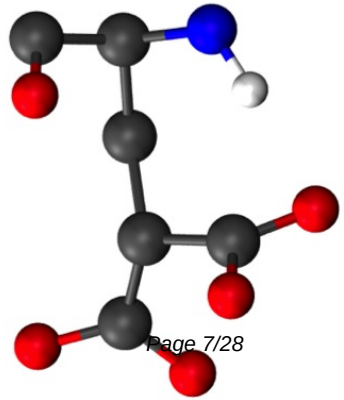
Glutamic acid (GLU)



protein adsorption on a COM surface

Calcium Oxalate Monohydrate (COM) surface

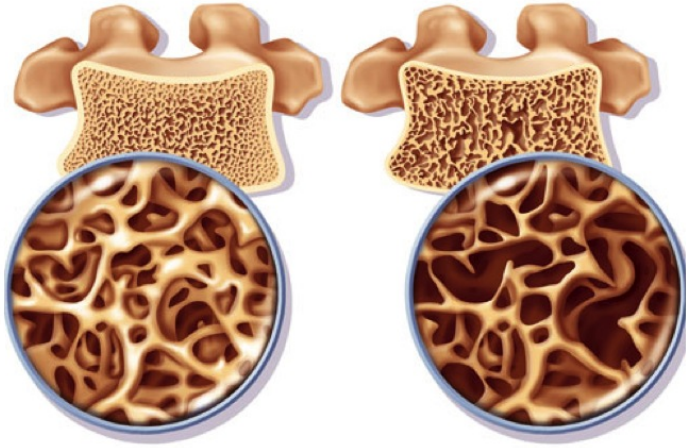
CaC_2O_4



gamma-carboxy-glutamic acid (GLA)

Biomineralization-related diseases

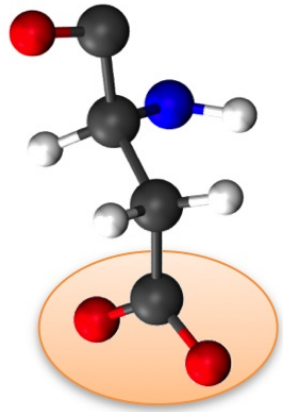
Hard tissues



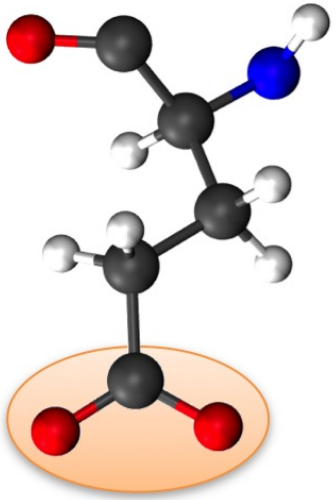
normal bone osteoporosis

Hydroxyapatite (HA) surface

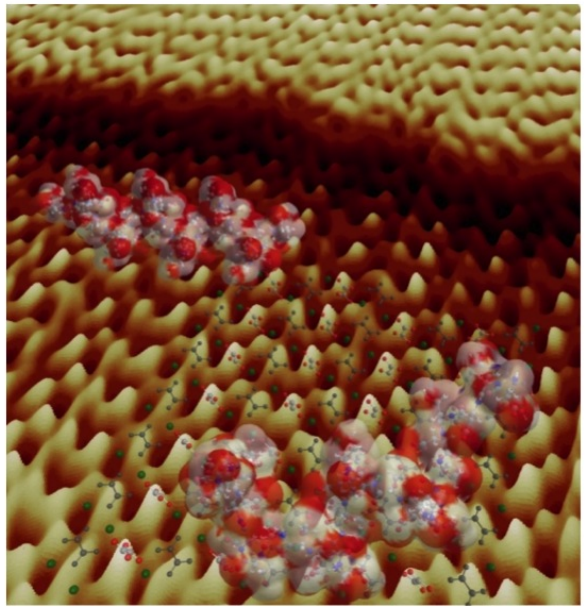
$Ca_5(PO_4)_3(OH)$



Aspartic acid (ASP)



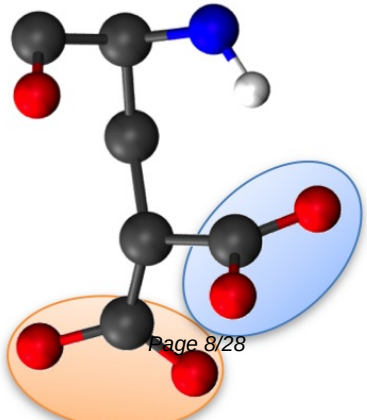
Glutamic acid (GLU)



protein adsorption on a COM surface

Calcium Oxalate Monohydrate (COM) surface

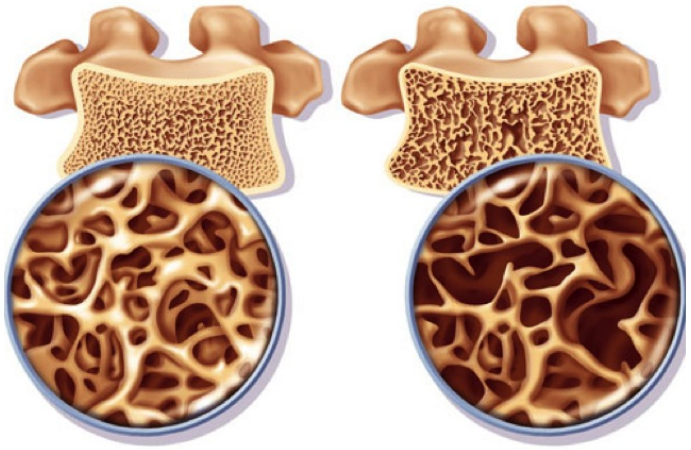
CaC_2O_4



gamma-carboxy-glutamic acid (GLA)

Biomineralization-related diseases

Hard tissues



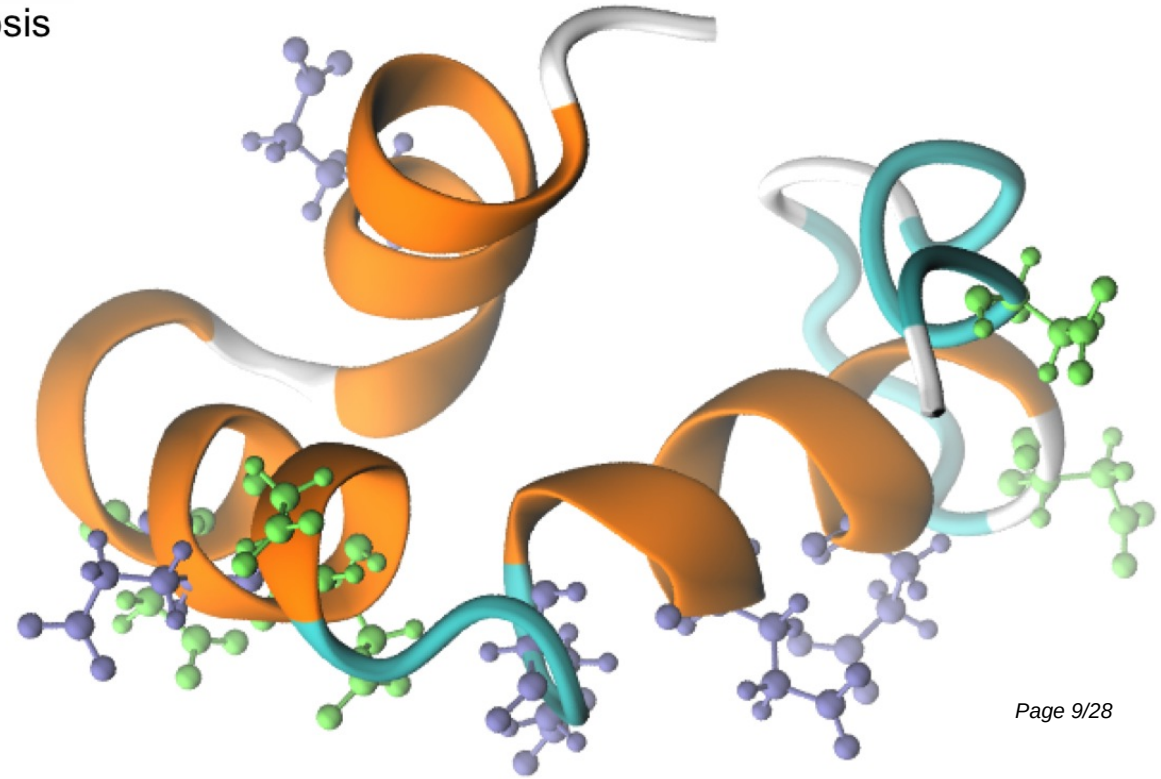
normal bone osteoporosis

Hydroxyapatite (HA) surface

$Ca_5(PO_4)_3(OH)$

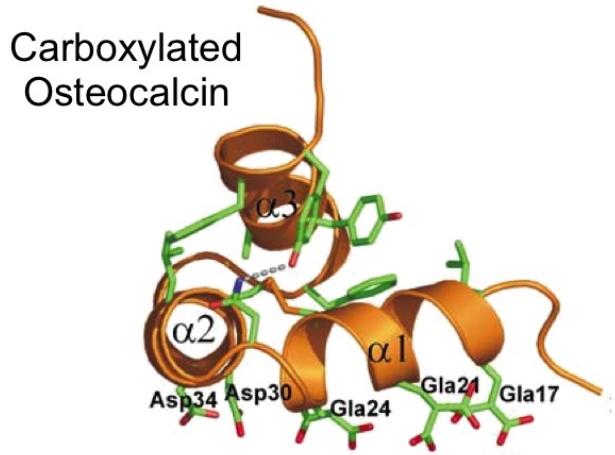
Osteocalcin (OC) protein

rich in ASP and GLU



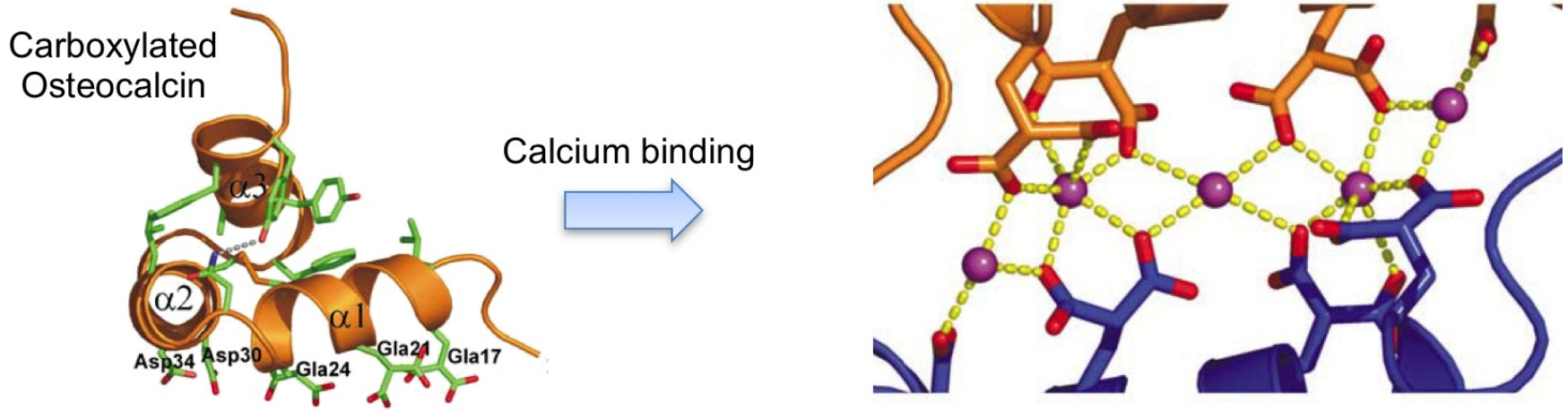
How is Hydroxyapatite lattice built by Osteocalcin protein?

Model of porcine Osteocalcin engaging an Hydroxyapatite crystal
based on a Ca^{2+} ion lattice match
(QQ. Hoang *et al.*, Nature 425, 977–980, 2003)



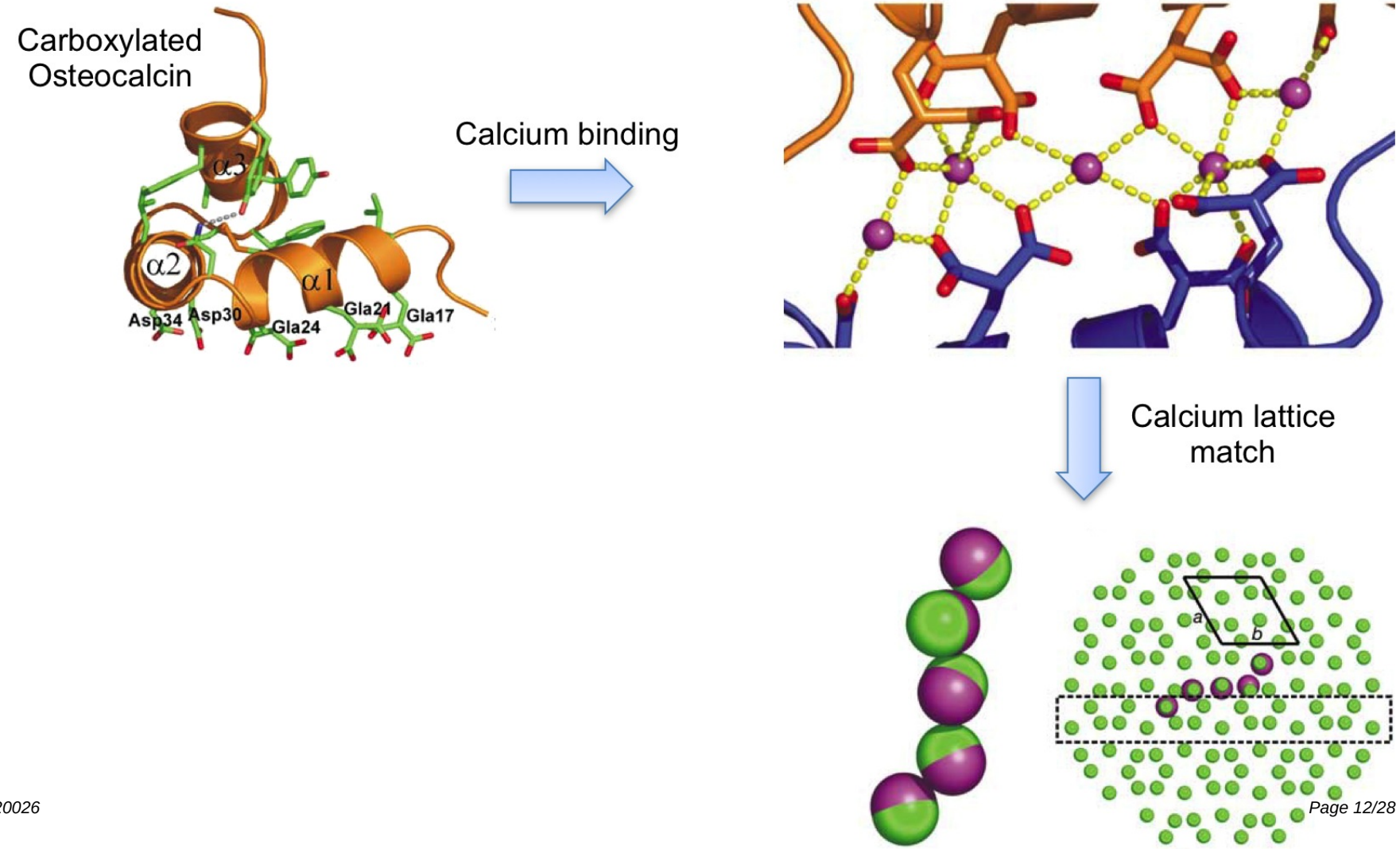
How is Hydroxyapatite lattice built by Osteocalcin protein?

Model of porcine Osteocalcin engaging an Hydroxyapatite crystal
based on a Ca^{2+} ion lattice match
(QQ. Hoang *et al.*, Nature 425, 977–980, 2003)



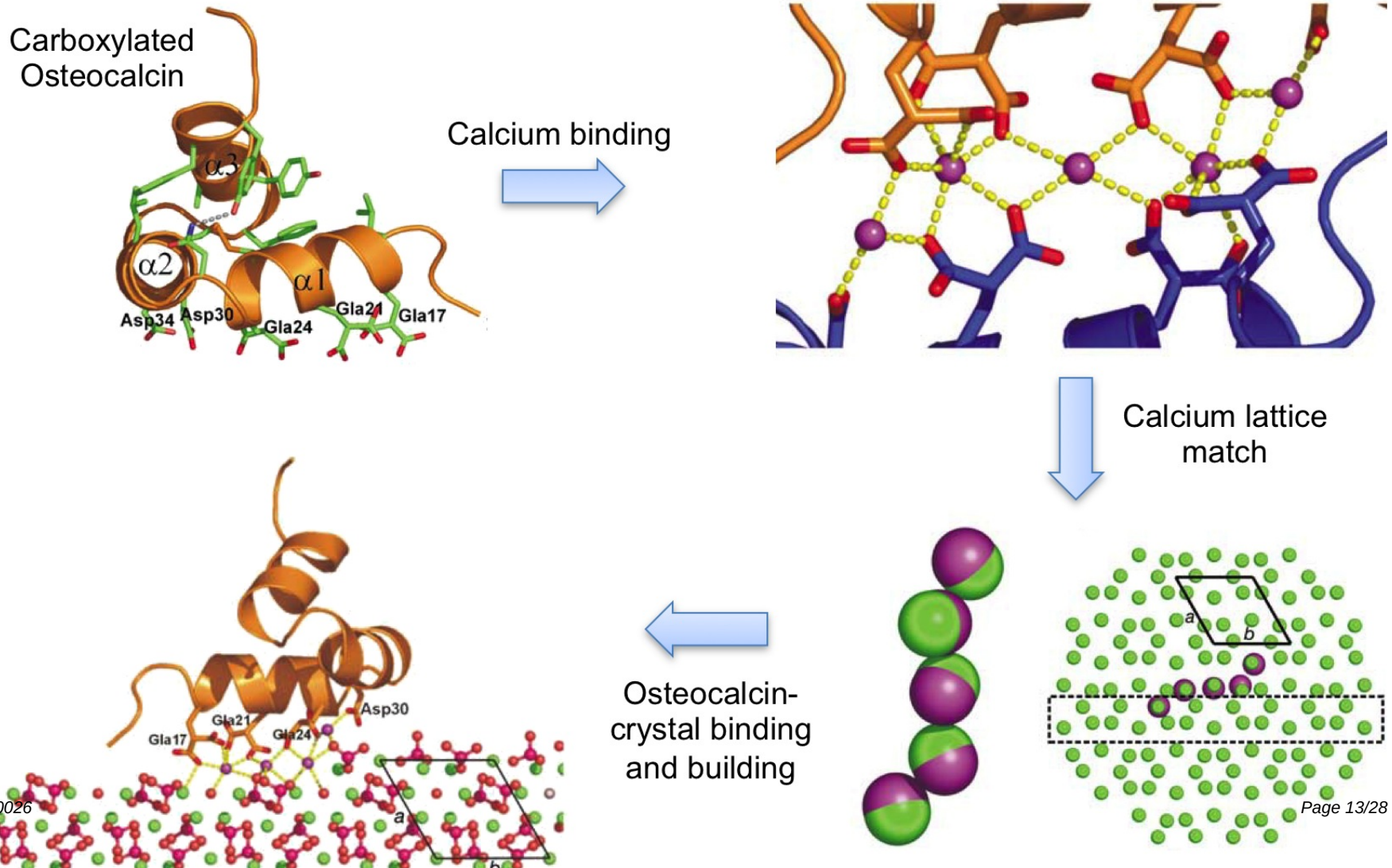
How is Hydroxyapatite lattice built by Osteocalcin protein?

Model of porcine Osteocalcin engaging an Hydroxyapatite crystal
based on a Ca^{2+} ion lattice match
(QQ. Hoang *et al.*, Nature 425, 977–980, 2003)

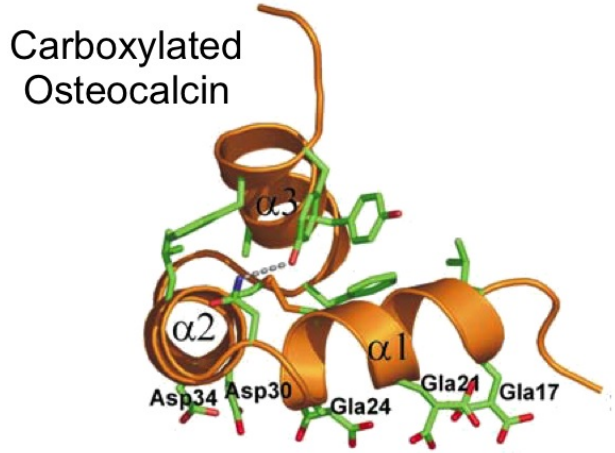


How is Hydroxyapatite lattice built by Osteocalcin protein?

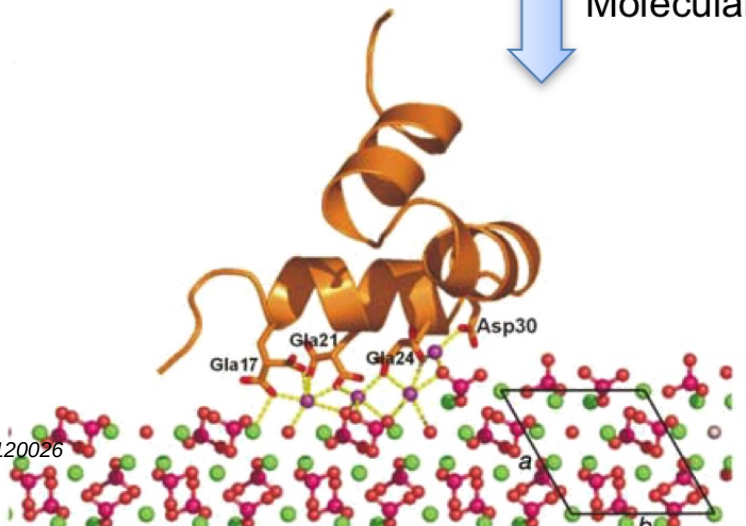
Model of porcine Osteocalcin engaging an Hydroxyapatite crystal
based on a Ca^{2+} ion lattice match
(QQ. Hoang *et al.*, Nature 425, 977–980, 2003)



How is Hydroxyapatite lattice built by Osteocalcin protein?

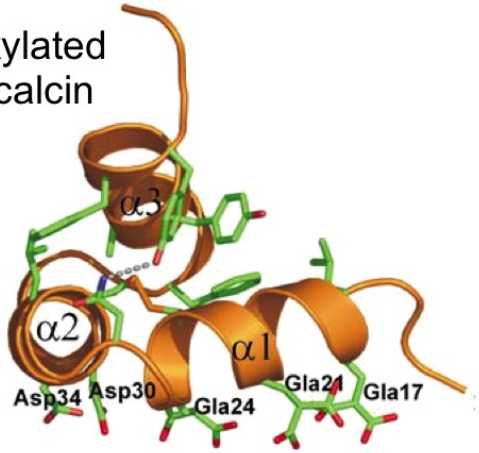


Molecular mechanism?

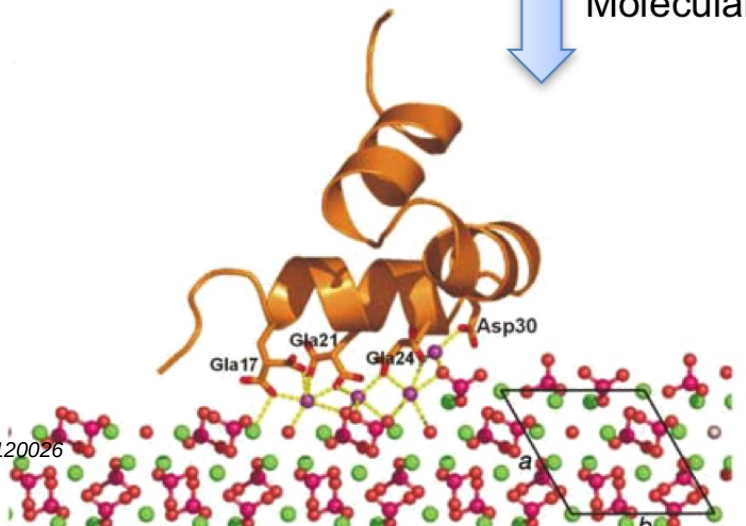


How is Hydroxyapatite lattice built by Osteocalcin protein?

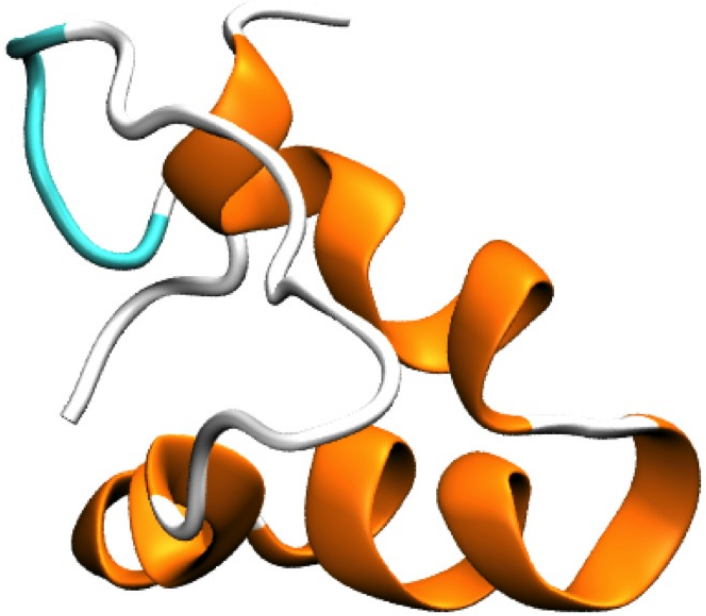
Carboxylated Osteocalcin

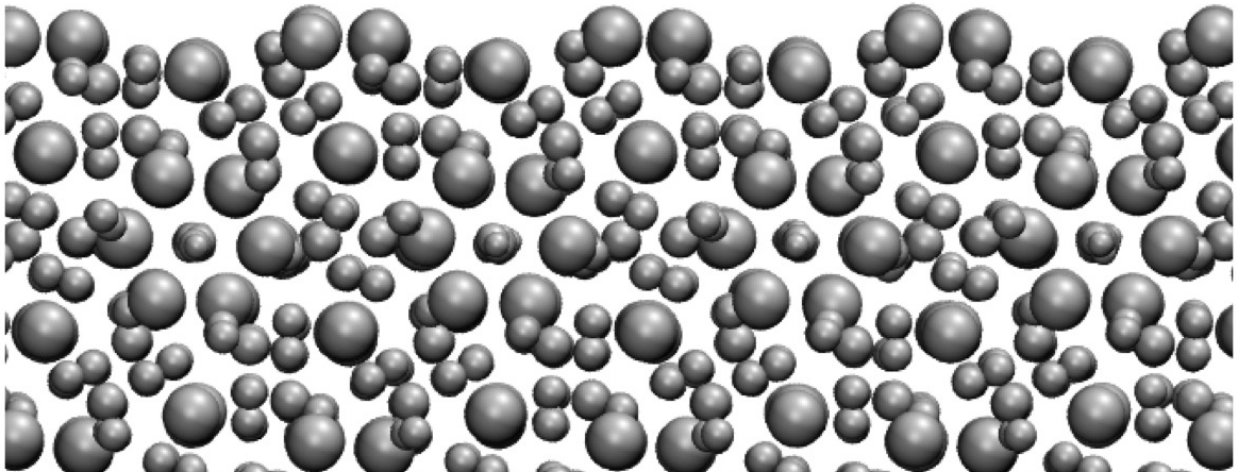


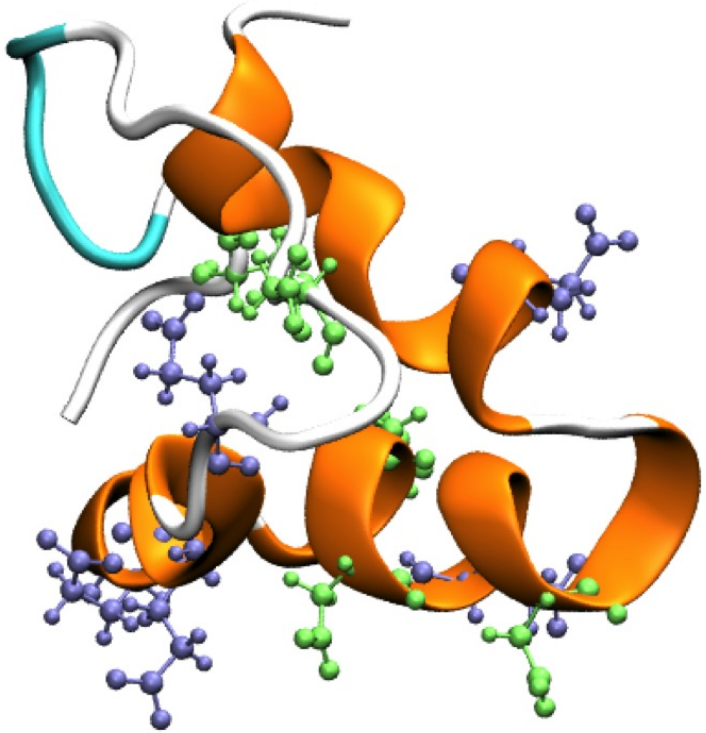
Molecular mechanism?

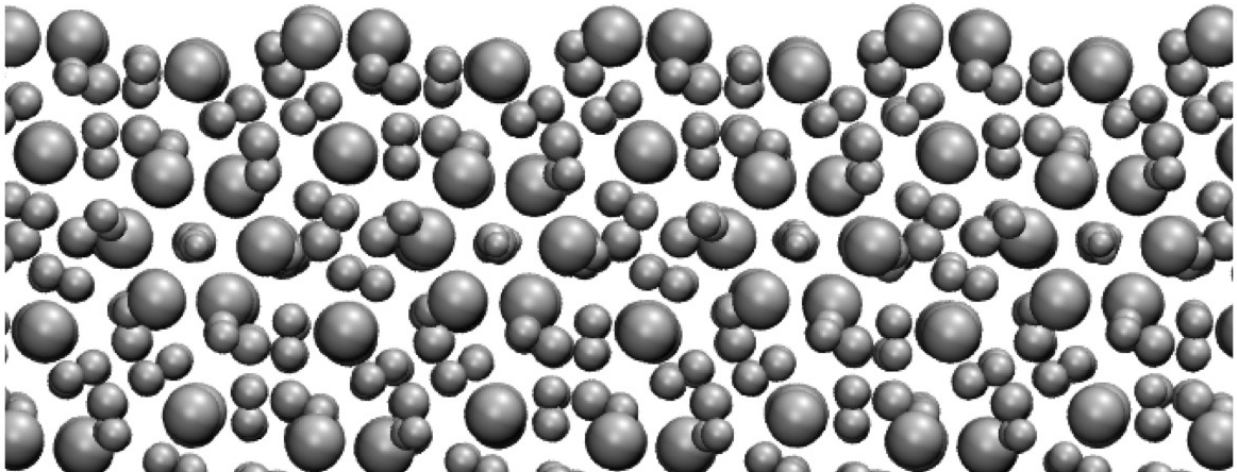


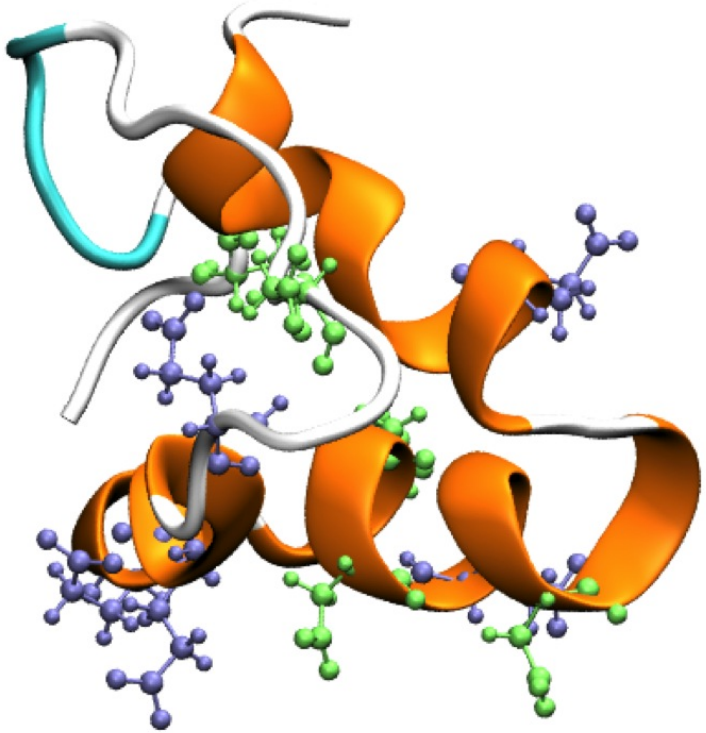
MOLECULAR SIMULATIONS

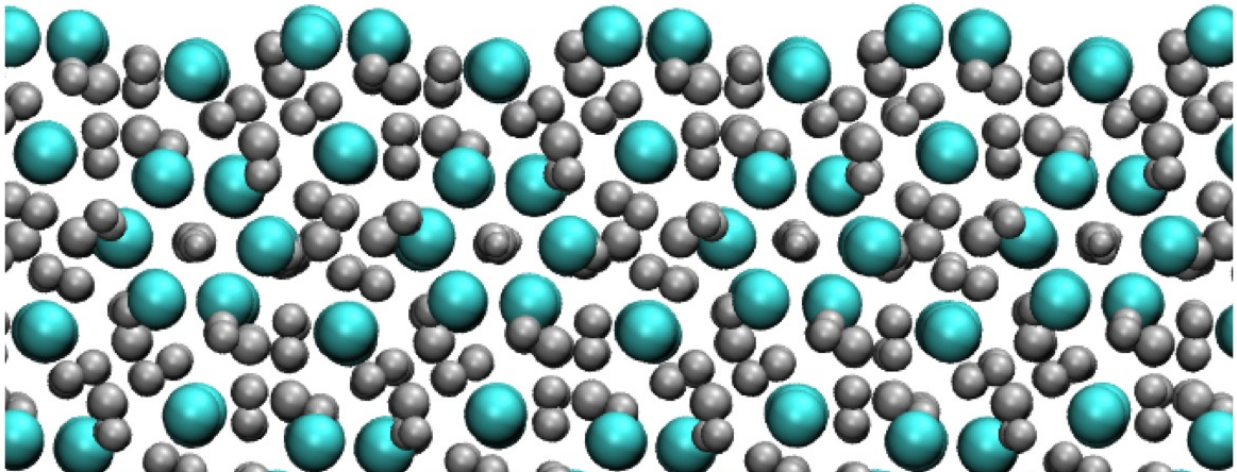


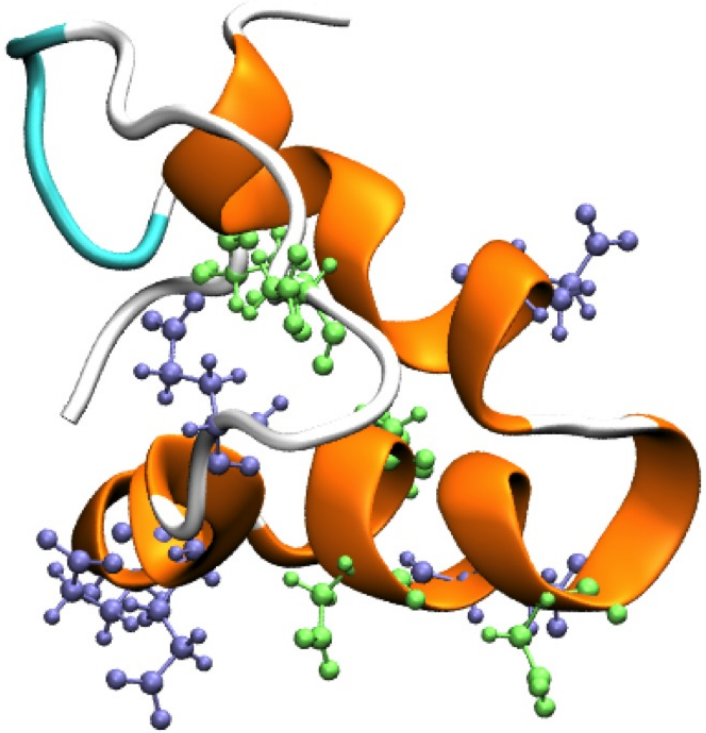


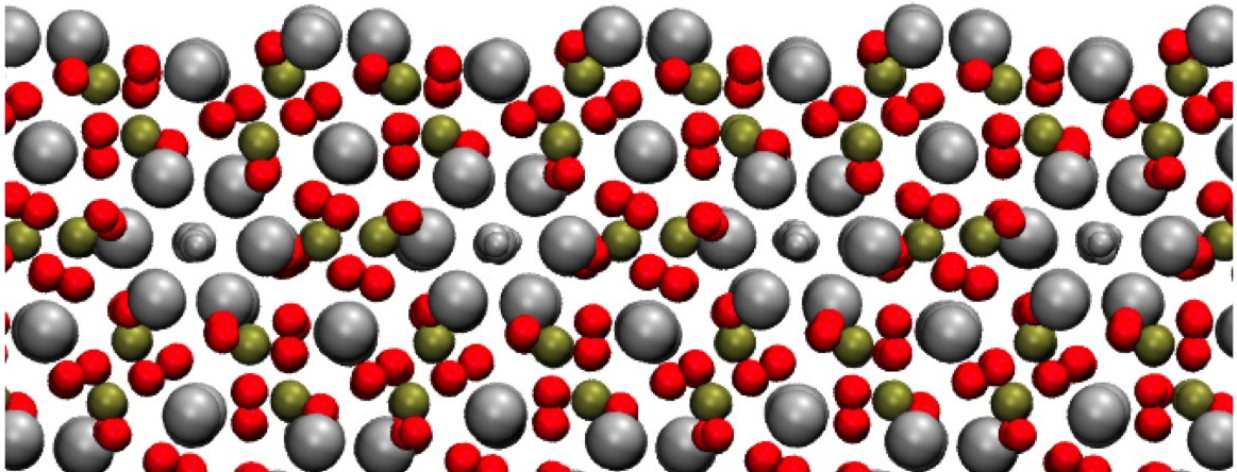


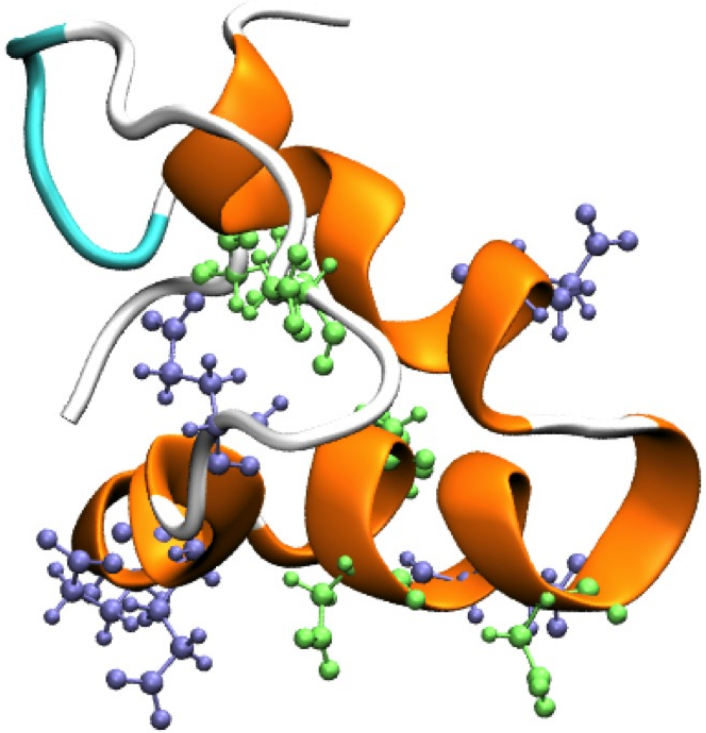


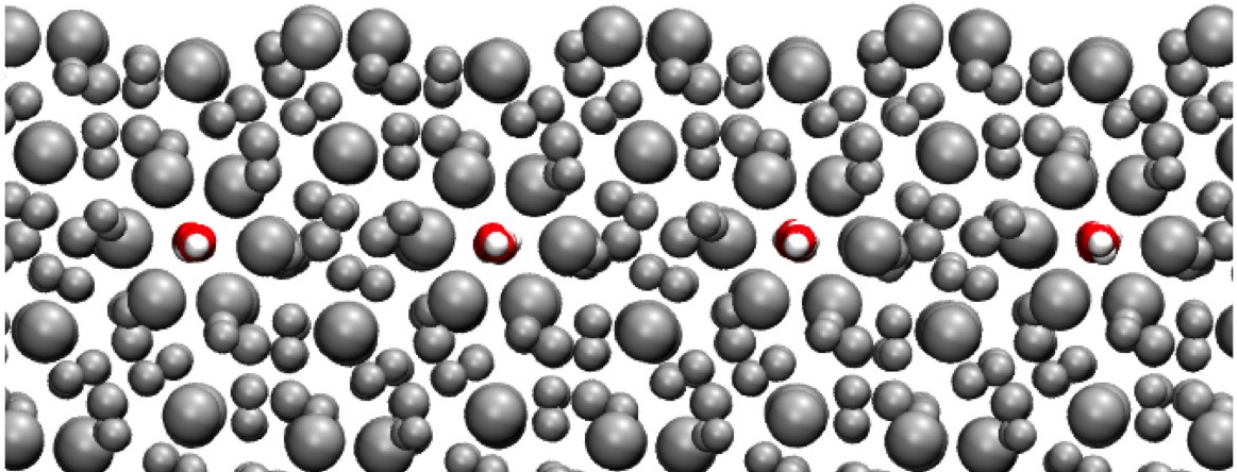


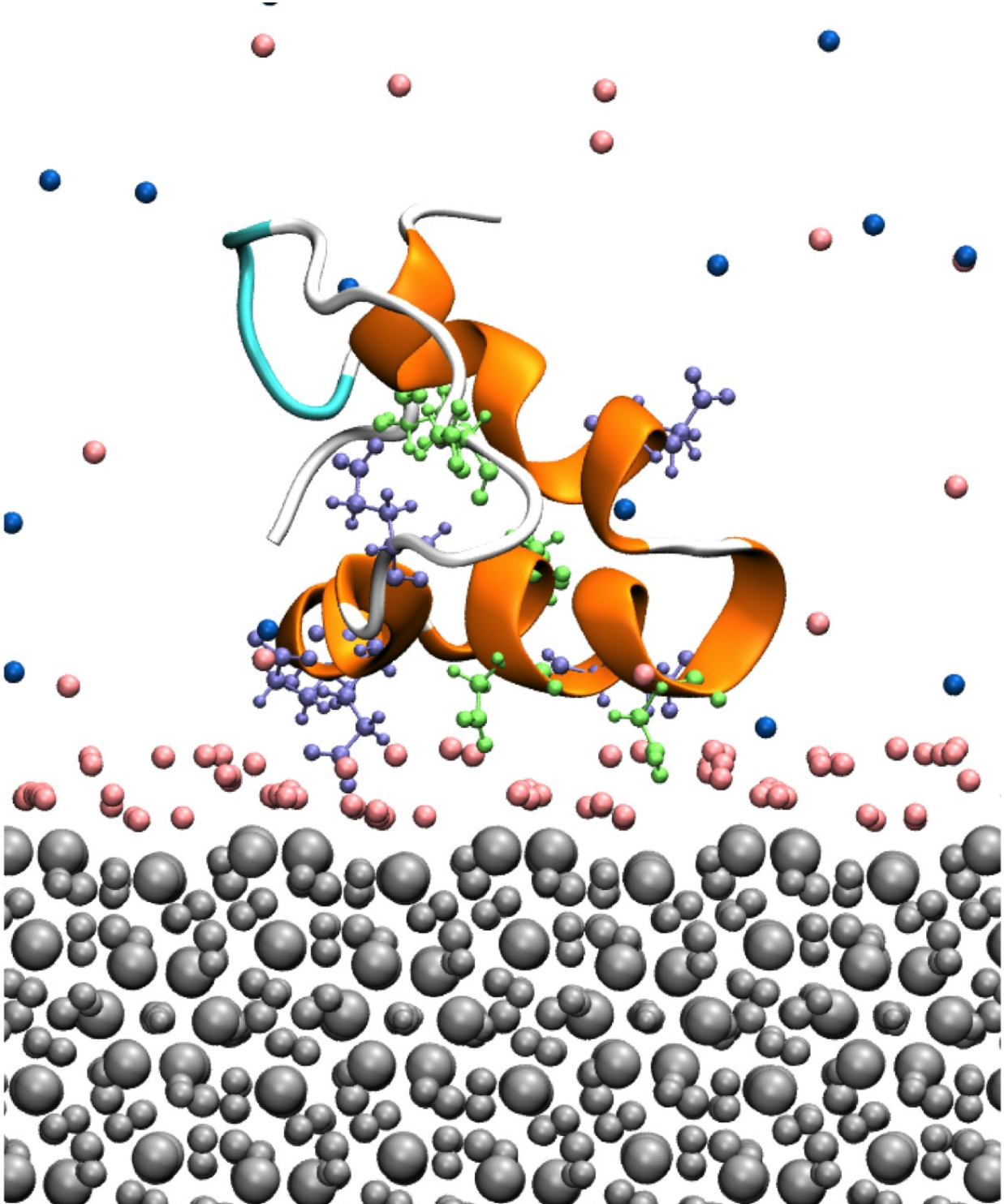


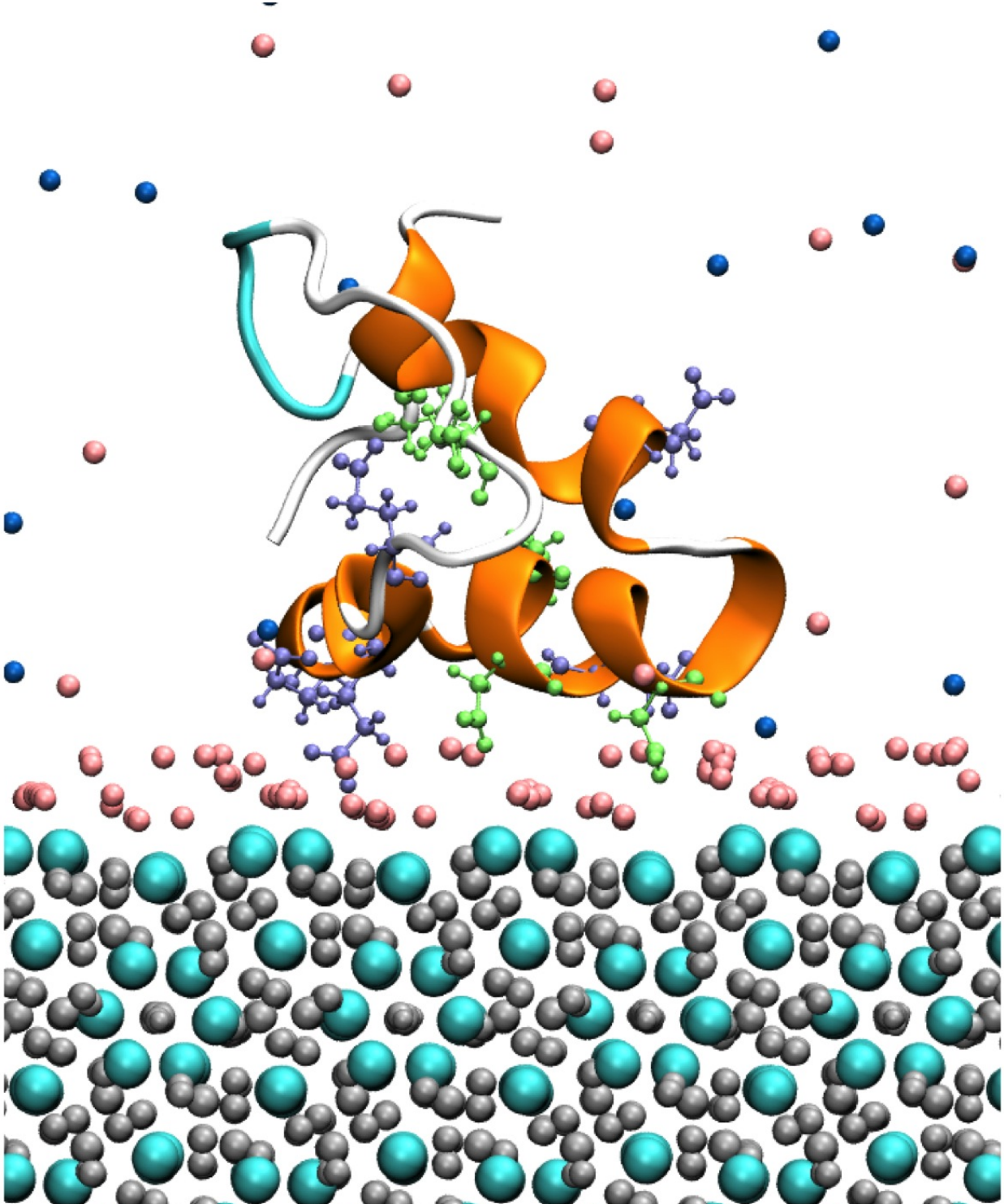




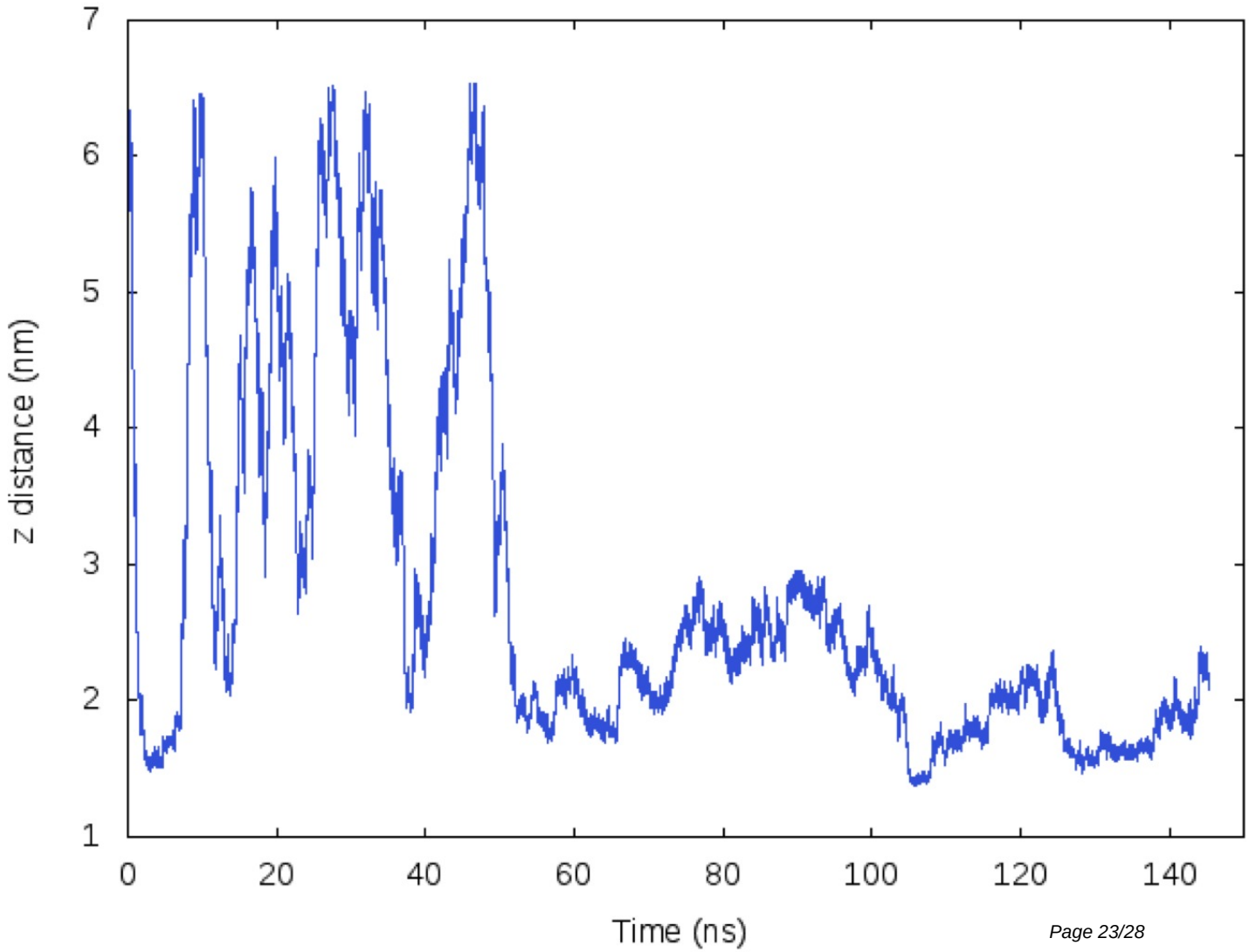




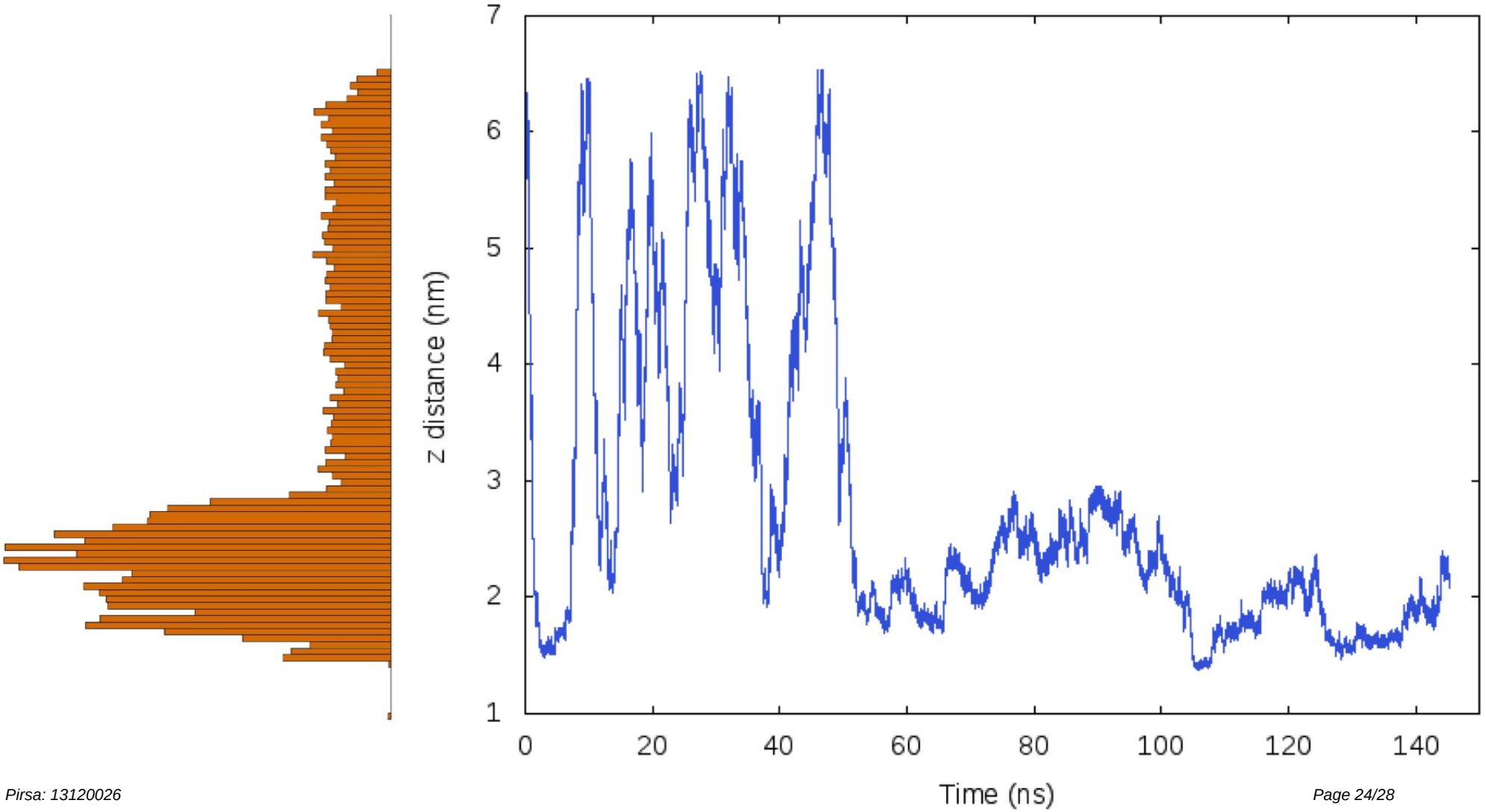




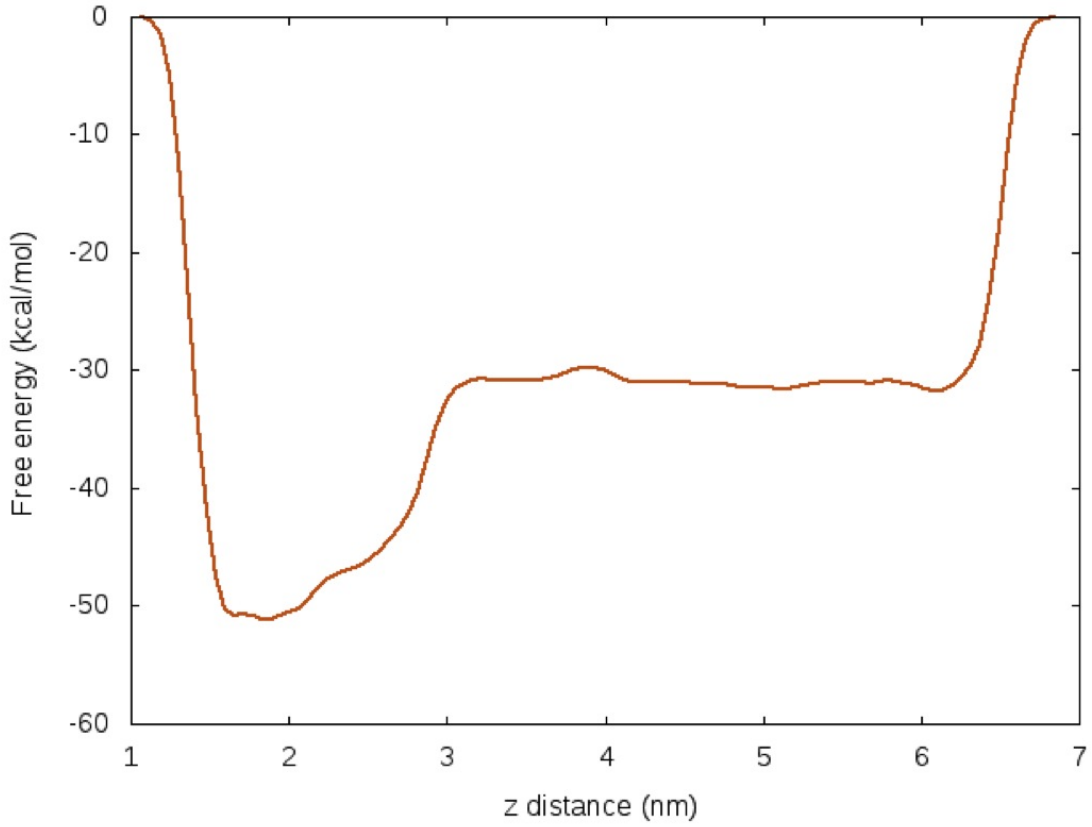
Binding of Osteocalcin to Hydroxyapatite surface by metadynamics simulations



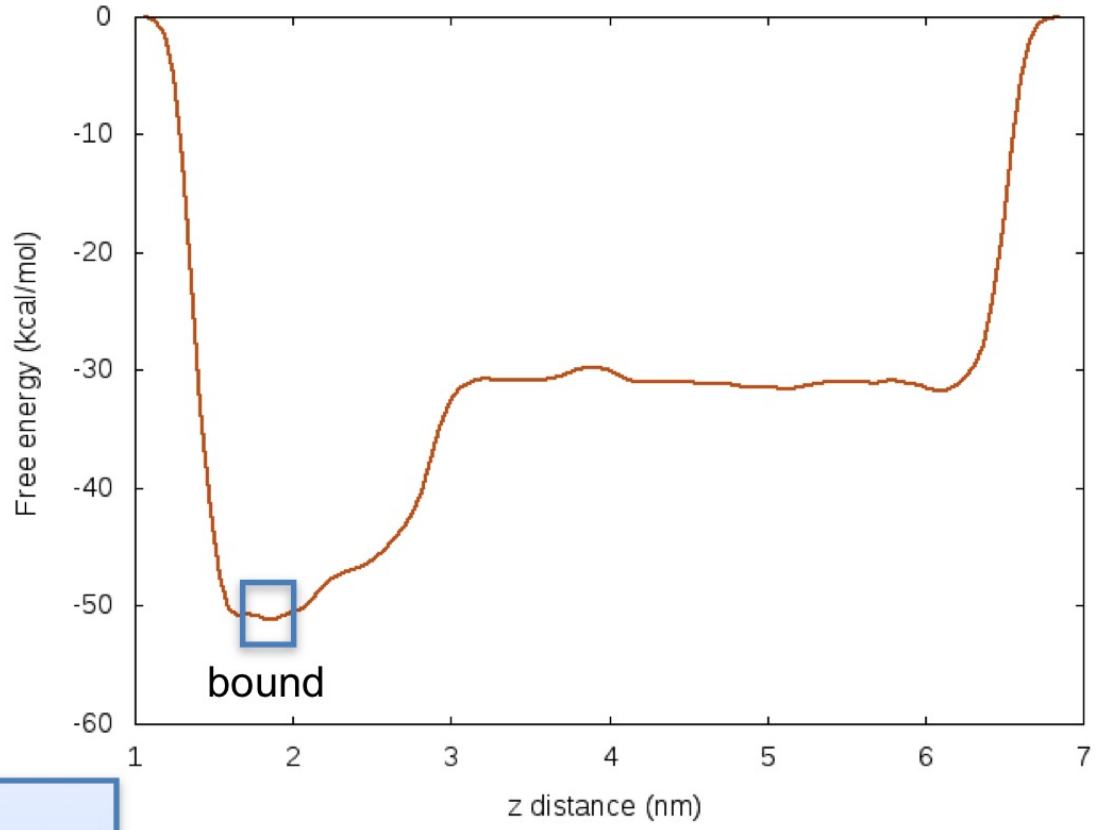
Binding of Osteocalcin to Hydroxyapatite surface by metadynamics simulations

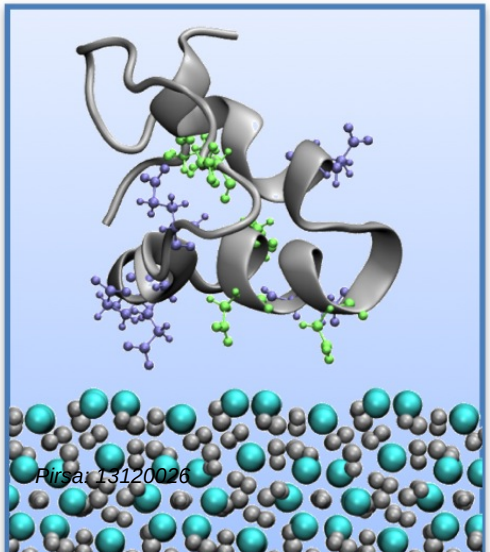


Free energy of Osteocalcin-Hydroxyapatite Binding



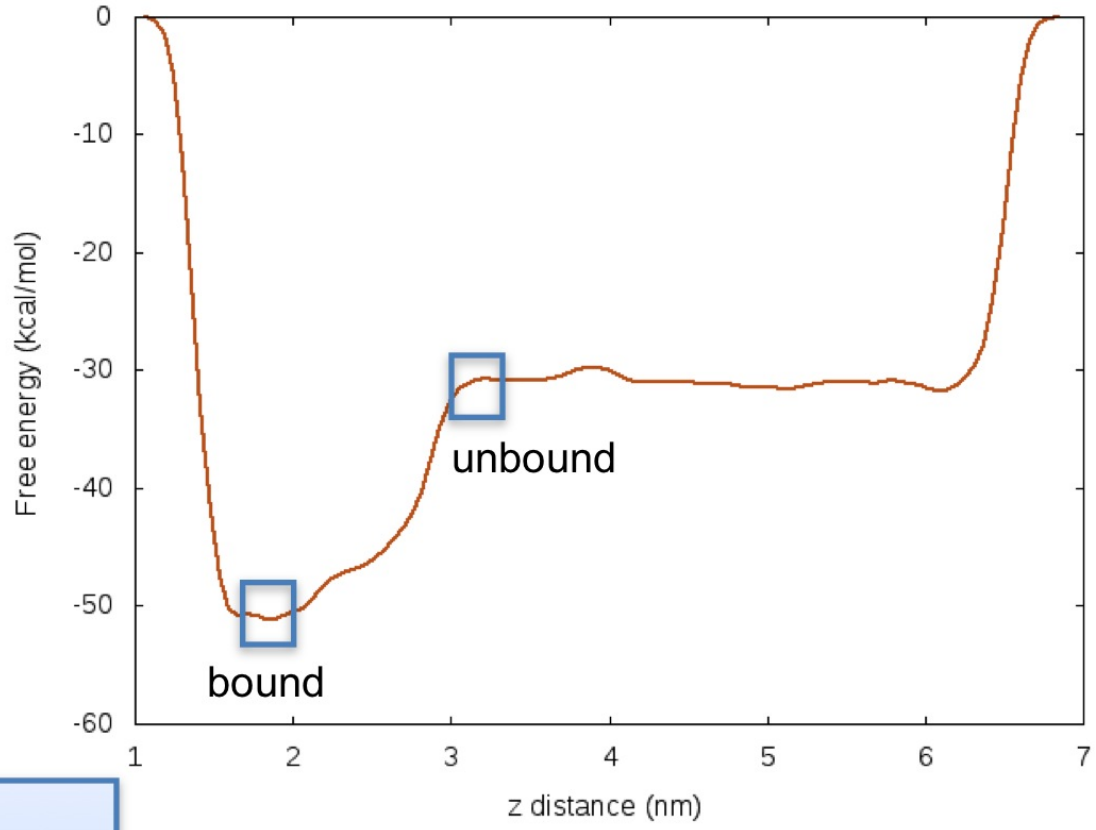
Free energy of Osteocalcin-Hydroxyapatite Binding

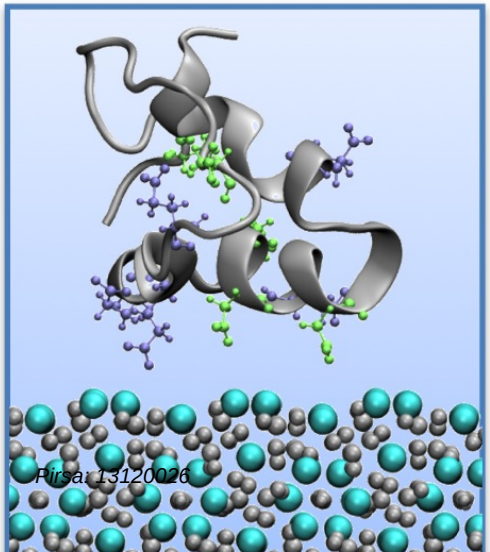




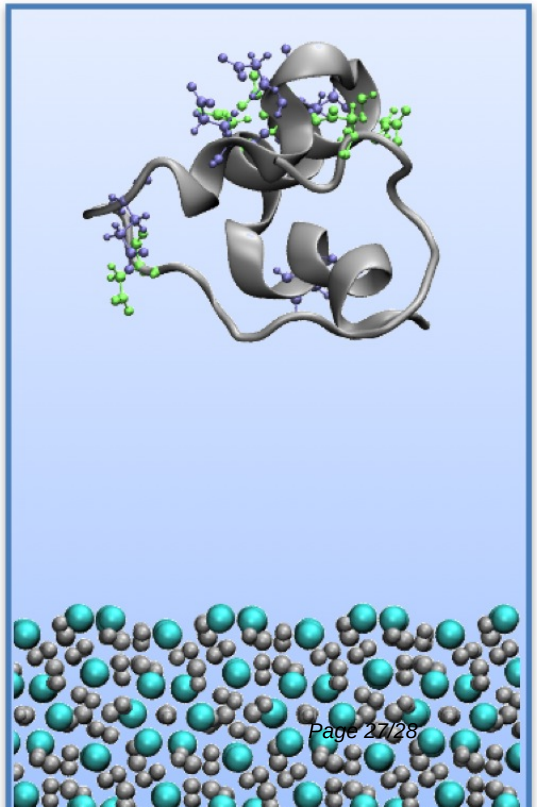
bound

Free energy of Osteocalcin-Hydroxyapatite Binding





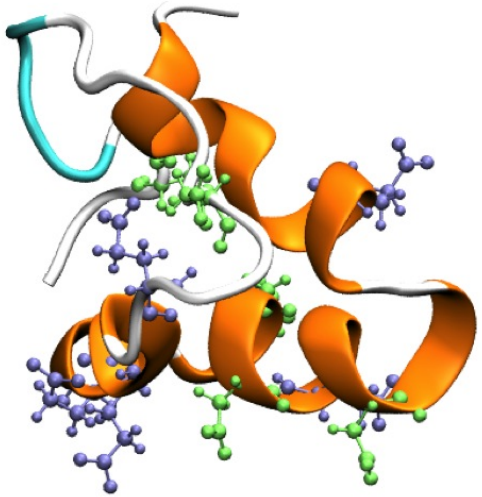
bound



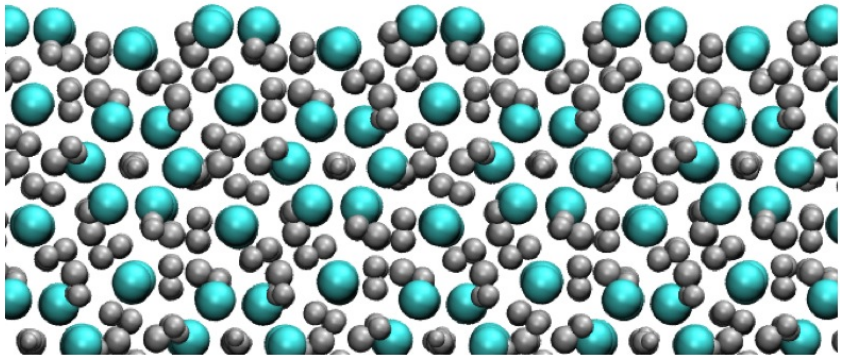
unbound

Summary

Osteocalcin plays an important role in the mineral phase of bone but the molecular mechanism is unclear.



Preliminary metadynamics simulations show that the bound state is more favorable than the unbound state.



During molecular simulations, charged residues (ASP, GLU, GLA) form key electrostatic interactions with the crystal surface.