How bone is organised

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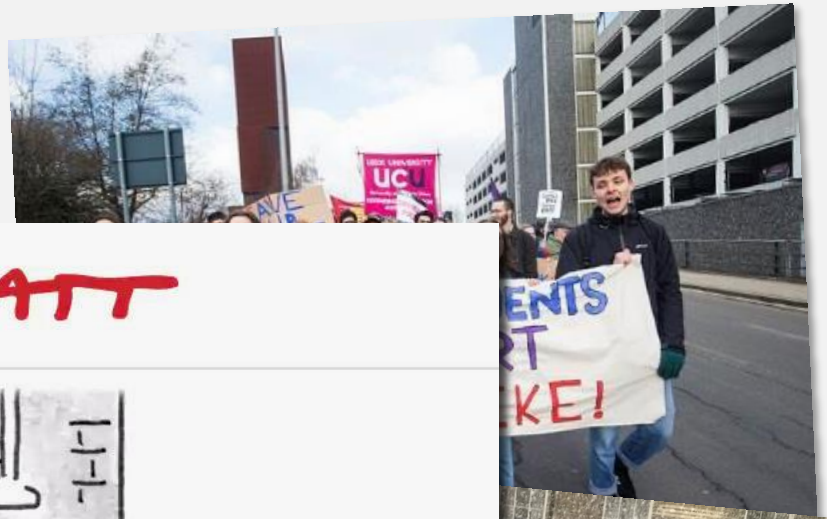
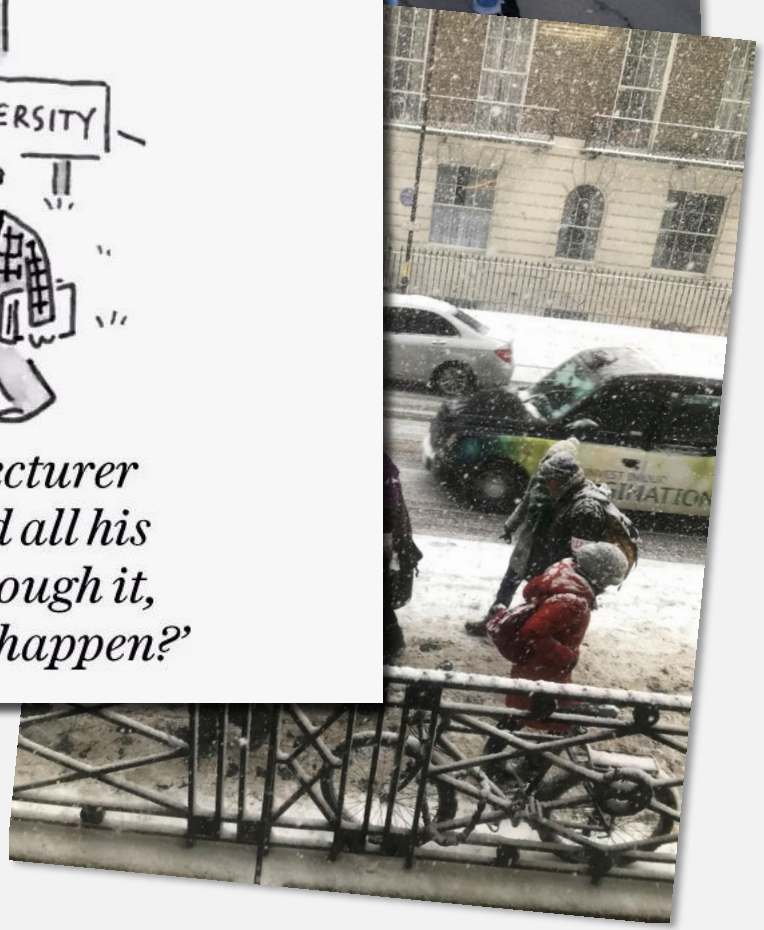
KBVR·SRBR
Bone Curriculum Symposium 2018



MATT

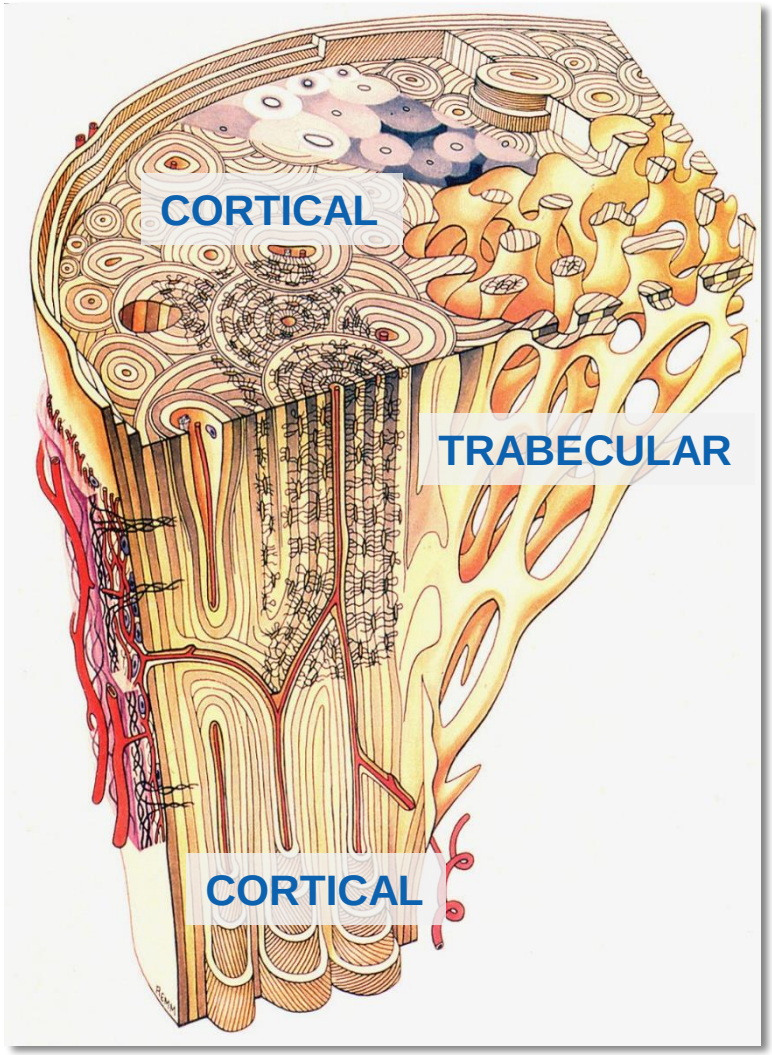
'If a philosophy lecturer goes on strike and all his students sleep through it, did the strike ever happen?'



Outline…

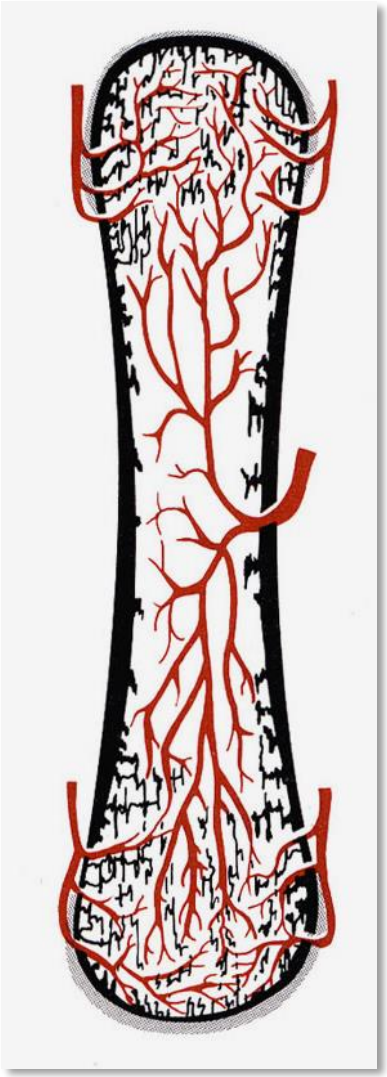
- Cortical / trabecular
- Vasculature
- Cells
- Composition
- Woven / lamellar
- Remodelling
- Collagen
- Mineralisation

Bone is a dynamic tissue

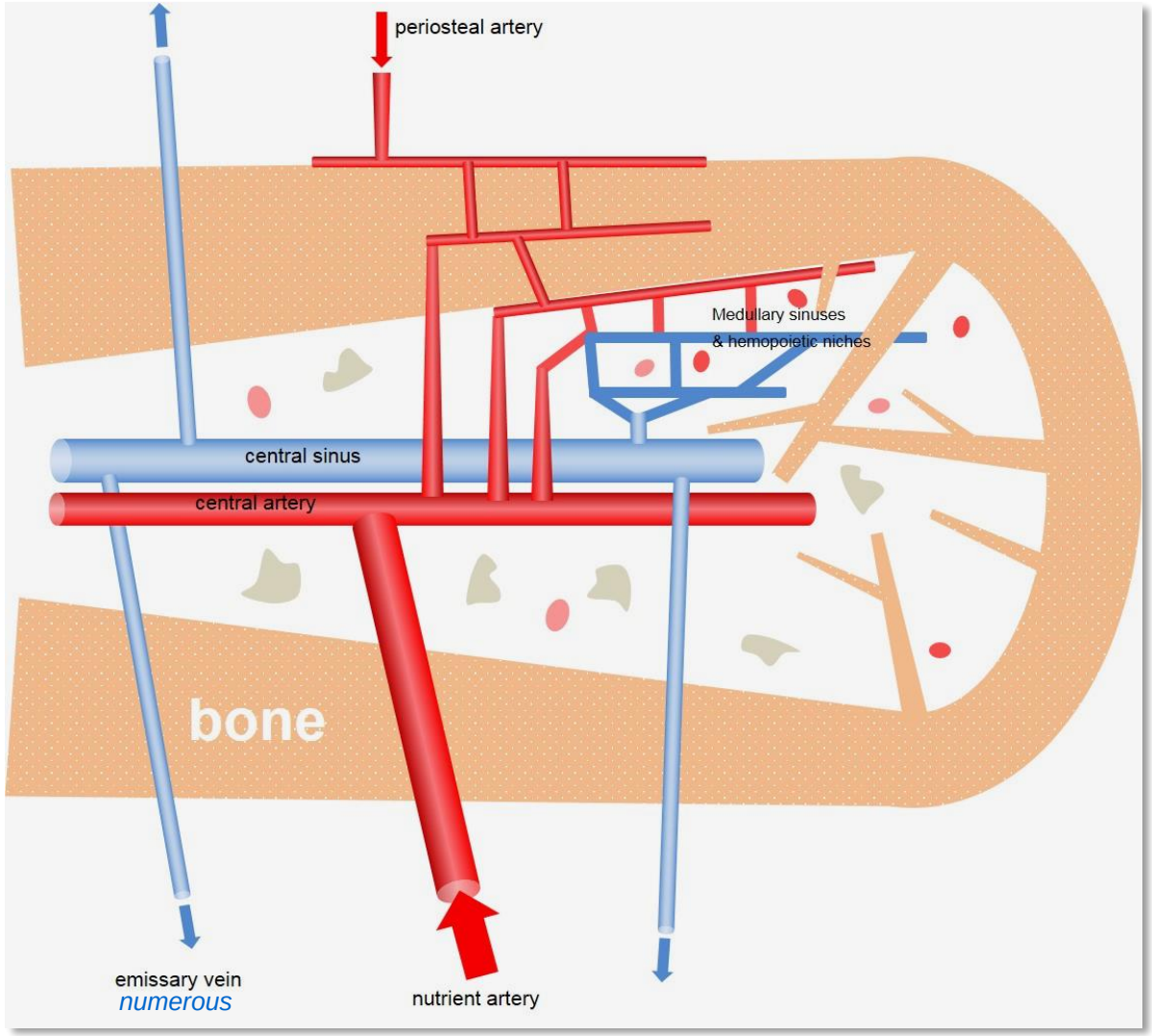


- Bone is highly vascular - gets about 7-8% of cardiac output
- Blood supply enables remodelling and repair
- Bone is innervated *(nerve fibres mainly associated with blood vessels)*
- Contrast with cartilage *(primitive, avascular, low cellularity & metabolic rate, limited repair capacity)*

Bone blood flow



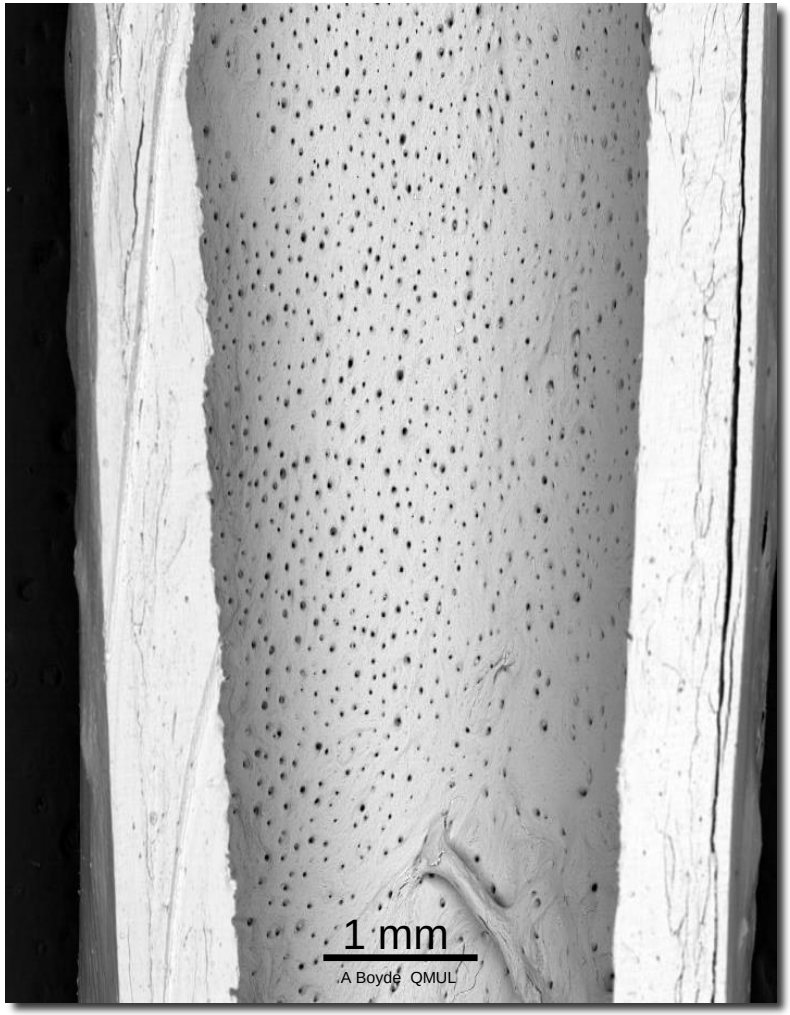
Alberts *et al* (2002) Molecular Biology of the Cell



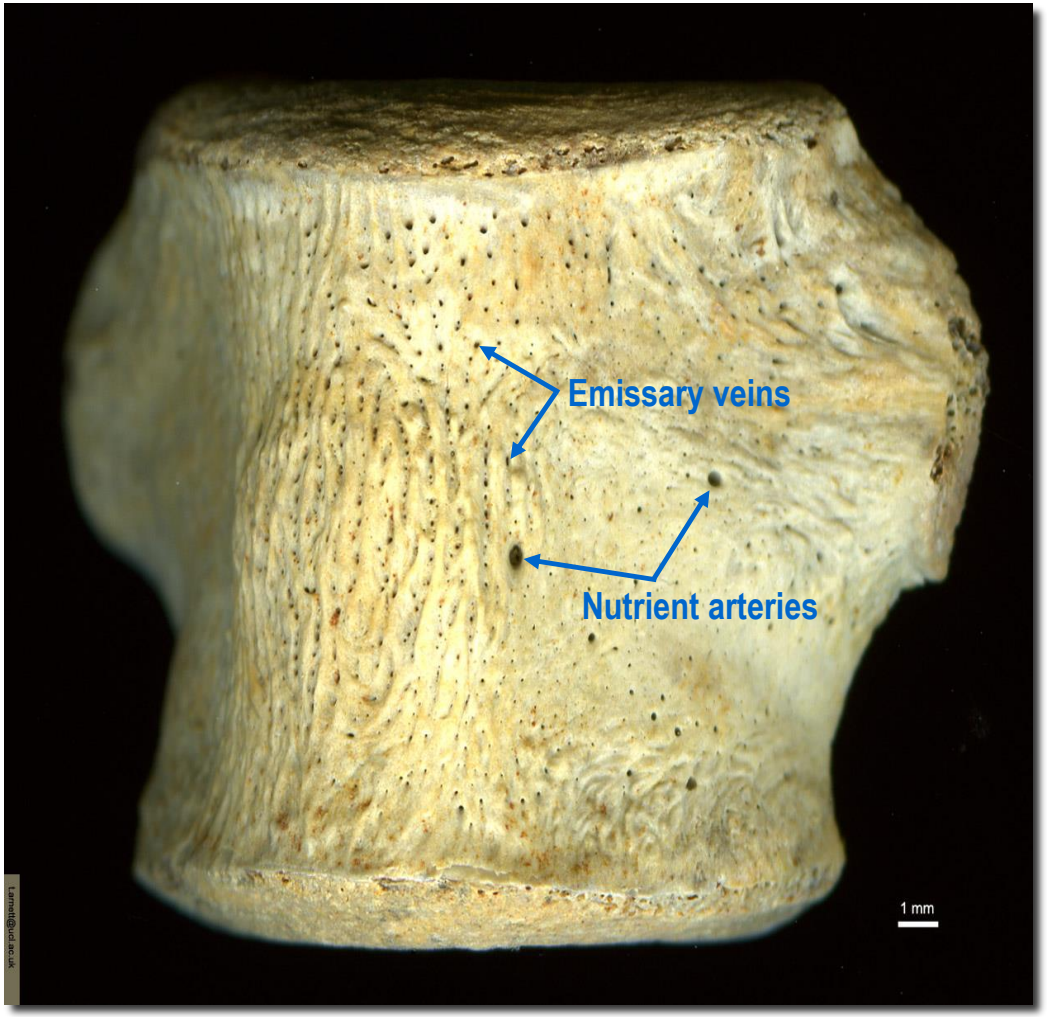
Marenzana & Arnett (2013) *Bone Research*

Vascular channels in bone

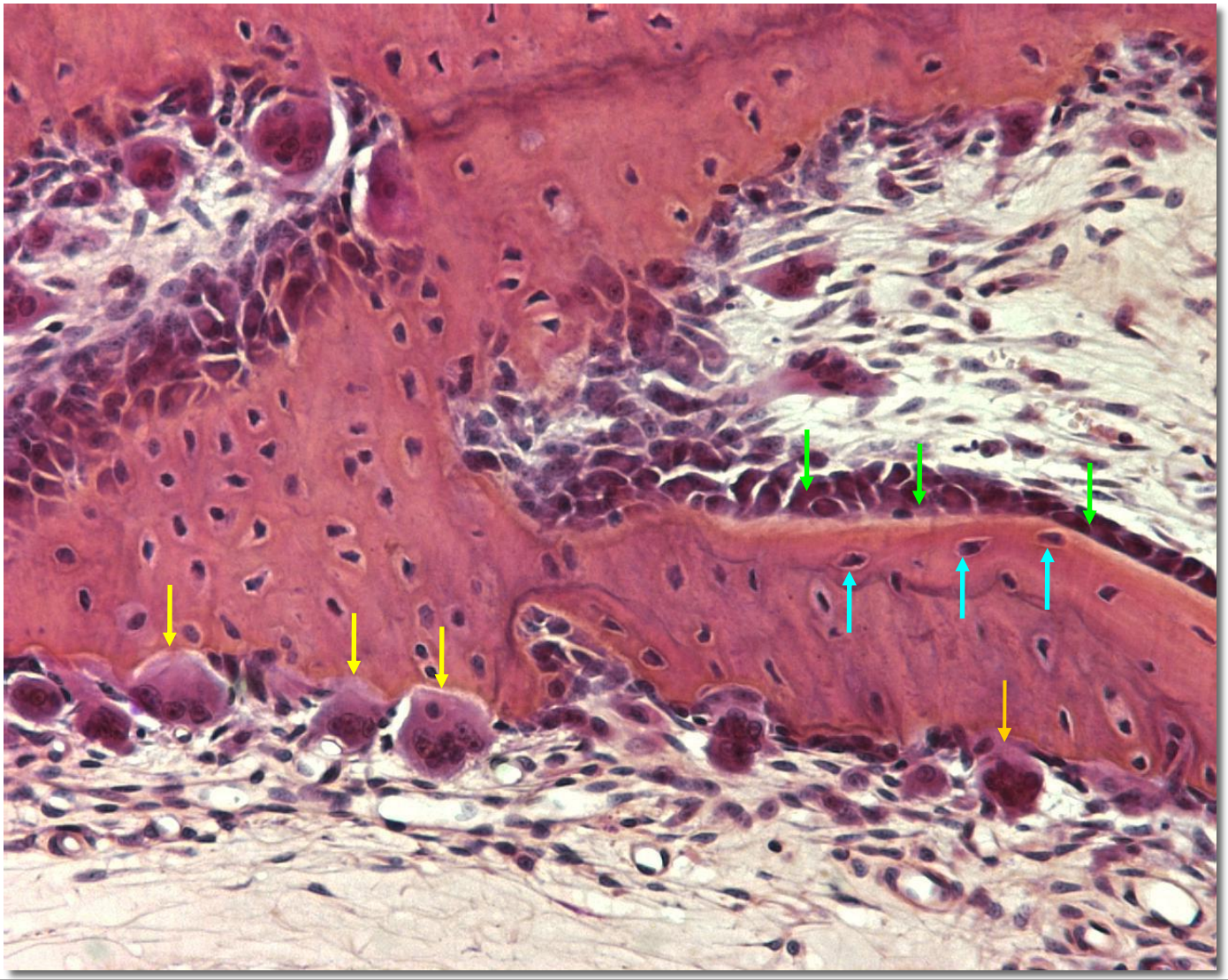
rat femur



small dinosaur tail vertebra (100 Myr)



Bone cells



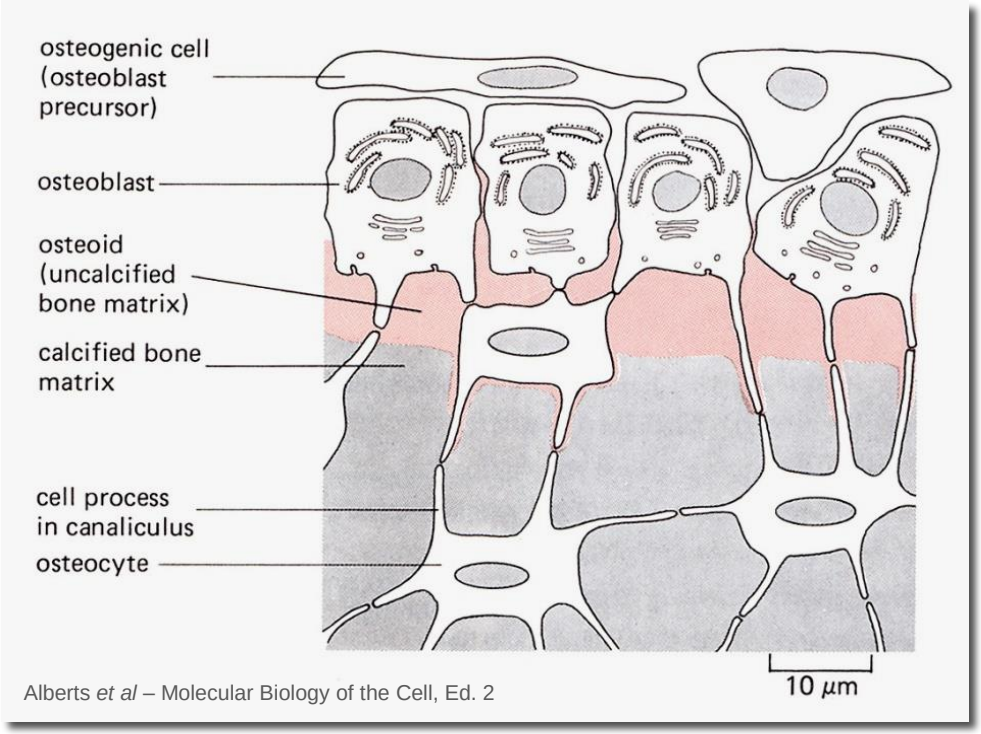
osteoclasts resorbing bone

osteocytes entombed in bone

osteoblasts forming bone

Bone cells - *osteoblasts*

- bone-forming cells of mesenchymal origin *ie*, connective tissue cells
- secrete organic matrix of bone (90% collagen 1)
- mineralise matrix with $Ca_4(PO_4)_3(OH)$ *(hydroxyapatatite)*

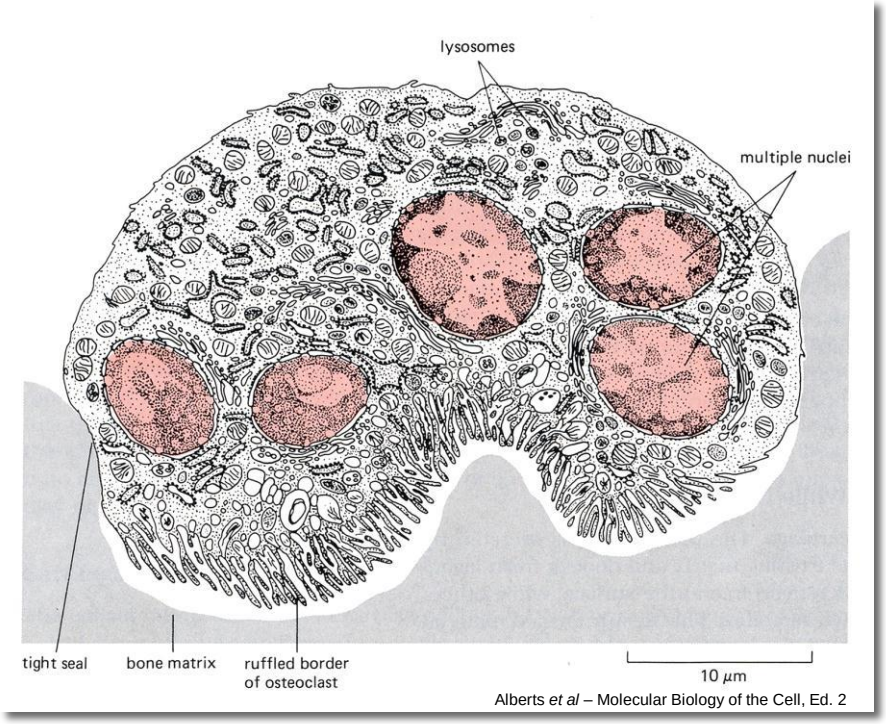


Alberts *et al* – Molecular Biology of the Cell, Ed. 2

- active or inactive (flattened) osteoblasts cover most bone surfaces
- incorporated into matrix & differentiate → osteocytes
  - network of cells present within all living bone

Bone cells - *osteoclasts*

- Multinucleated, motile bone-resorbing (destroying) cells
- Formed by fusion of pro-monocytic precursors present in marrow and circulation
- Specialised organ of resorption ('ruffled border') adjacent to bone surface



Alberts *et al* – Molecular Biology of the Cell, Ed. 2

- Ruffled border pumps acid (via H^+-ATPase) to dissolve bone mineral and enzymes (mainly cathepsin K) to degrade collagenous matrix

Bone matrix

- bone is a composite material
- organic component is ~90% type I collagen
  - *structural protein providing strength, flexibility*
- remaining 10% of organic component is complex mixture of proteins, including growth factors, osteocalcin, osteonectin, osteopontin, glycoproteins; all produced by osteoblasts, along with type I collagen

Bone matrix - 2

- organic matrix is mineralised after secretion

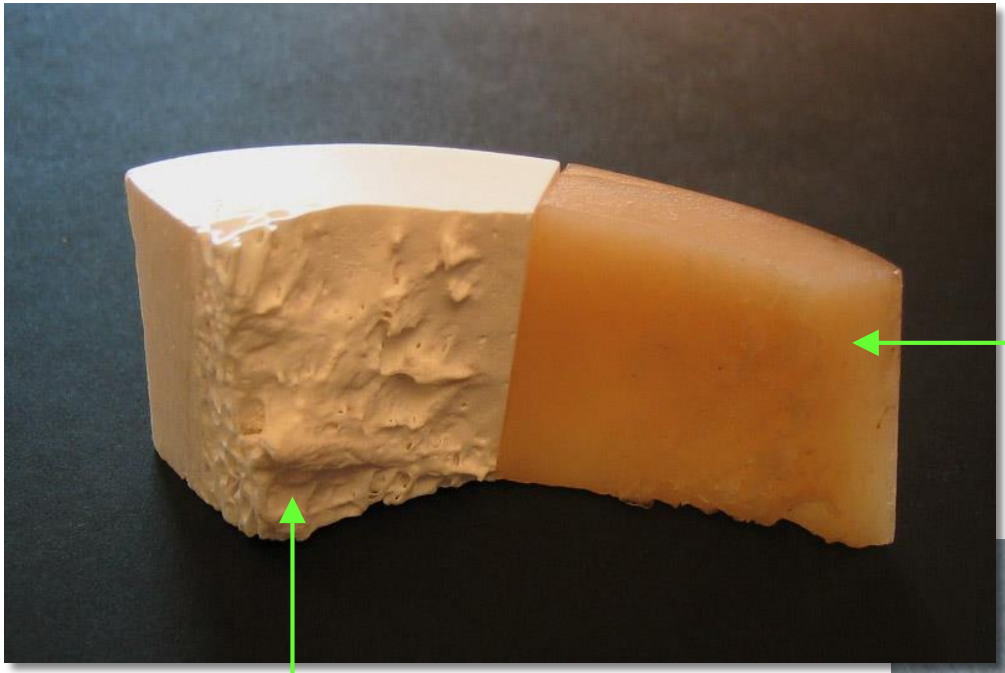
  – *unmineralised matrix = "osteoid"*

- mineral component is hydroxyapatite – $Ca_5 (PO_4)_3 (OH)$

  - tiny crystals impregnate & surround collagen fibres

  – *provides rigidity, resistance to compression*

Bone composition



Treated with hydrochloric acid to dissolve mineral ($Ca_{10}(PO_4)_6(OH)_2$)

leaves collagen component intact

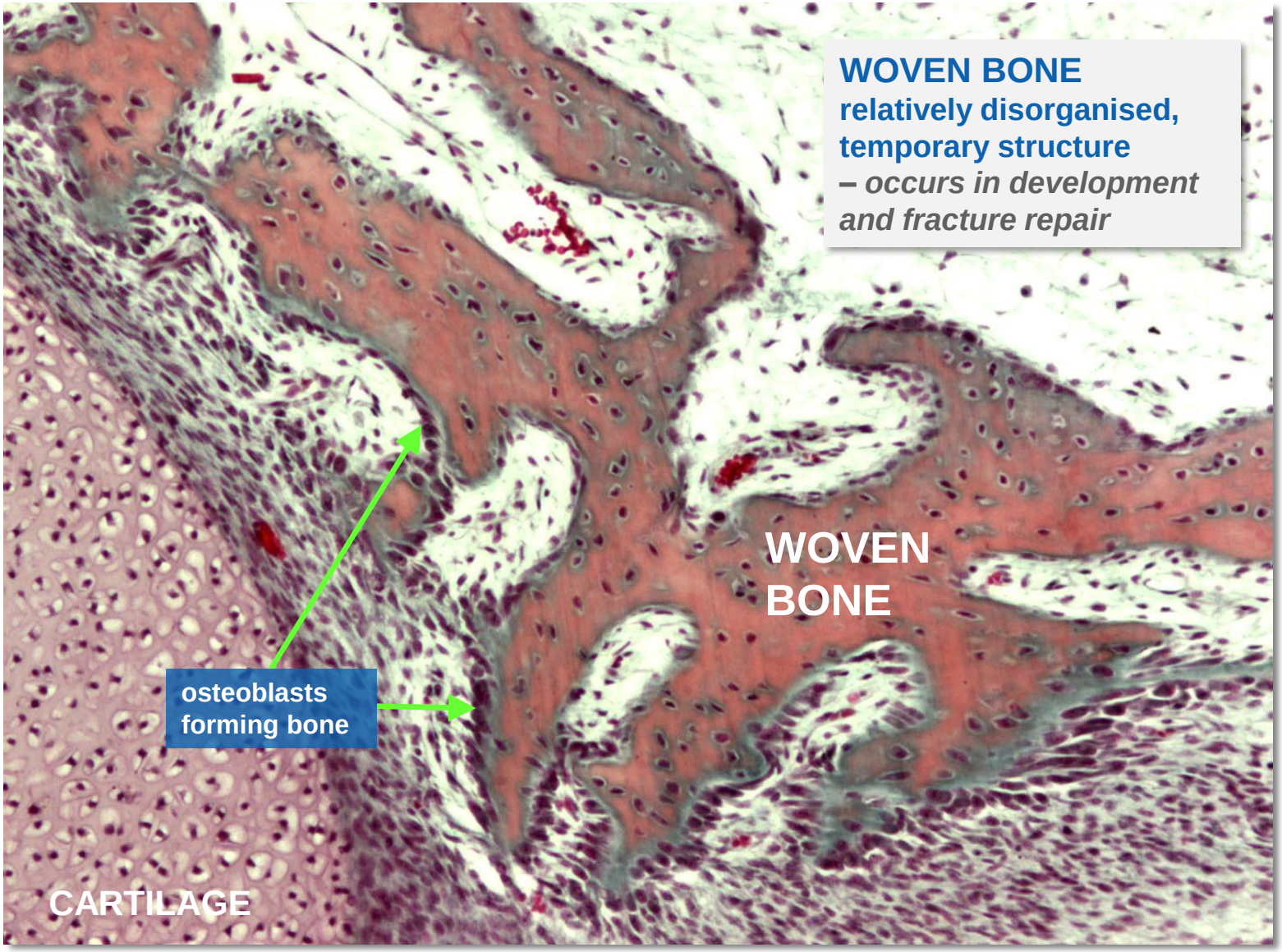
Treated with bleach (hypochlorite) to digest collagen

leaves mineral component intact

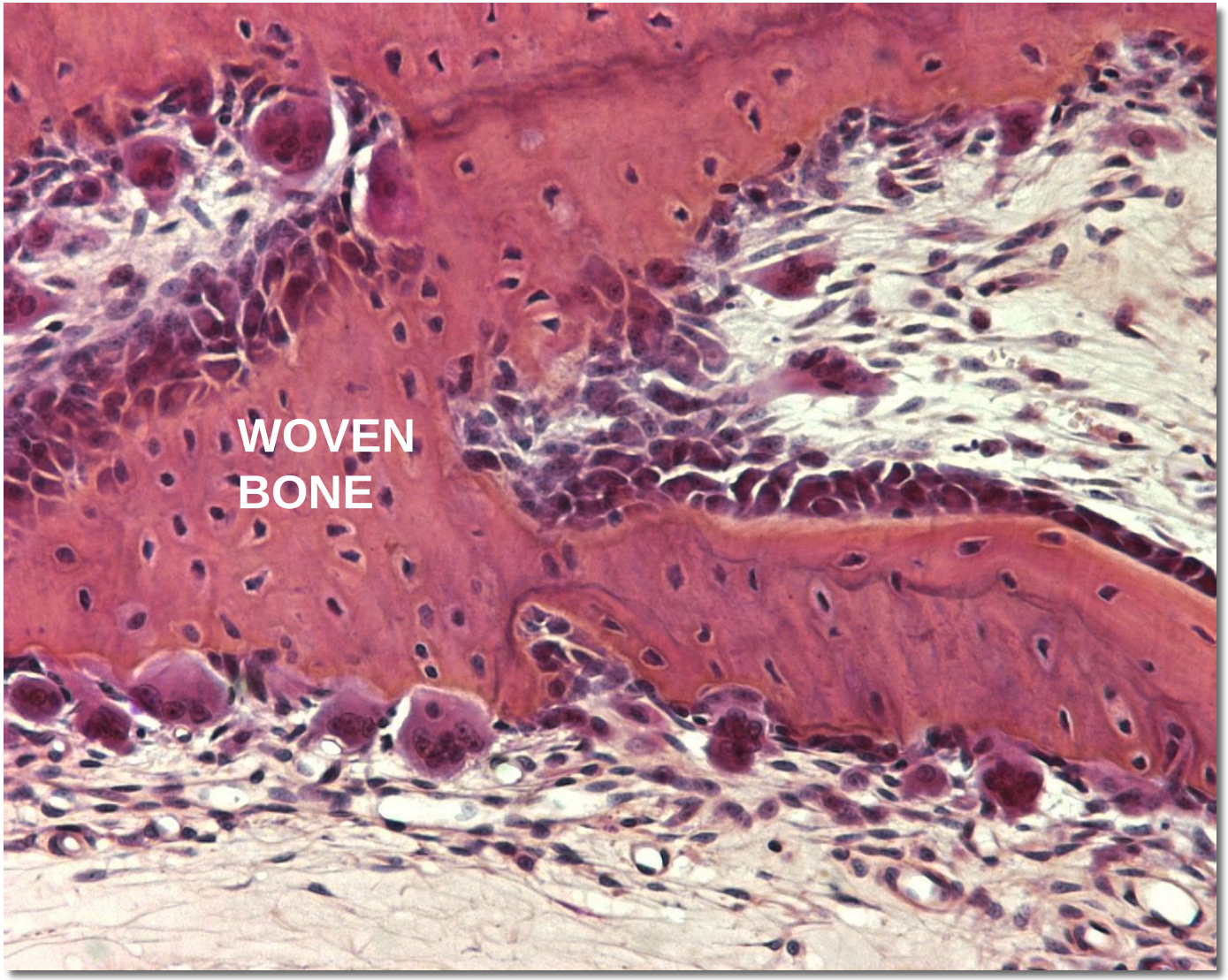
Two types of bone

Woven *(immature, fracture)*	**Lamellar** *(mature, adult)*
large, rounded osteocytes	smaller, flattened osteocytes
osteocytes irregularly spaced	osteocytes regularly spaced
randomly oriented collagen fibres	collagen fibres show regular, “plywood” orientation – *confers strength*
variable collagen fibre diameter	regular collagen fibre diameter
rapid matrix mineralisation	delayed matrix mineralisation (few days)
forms rapidly	forms slowly
rapid turnover	slow turnover

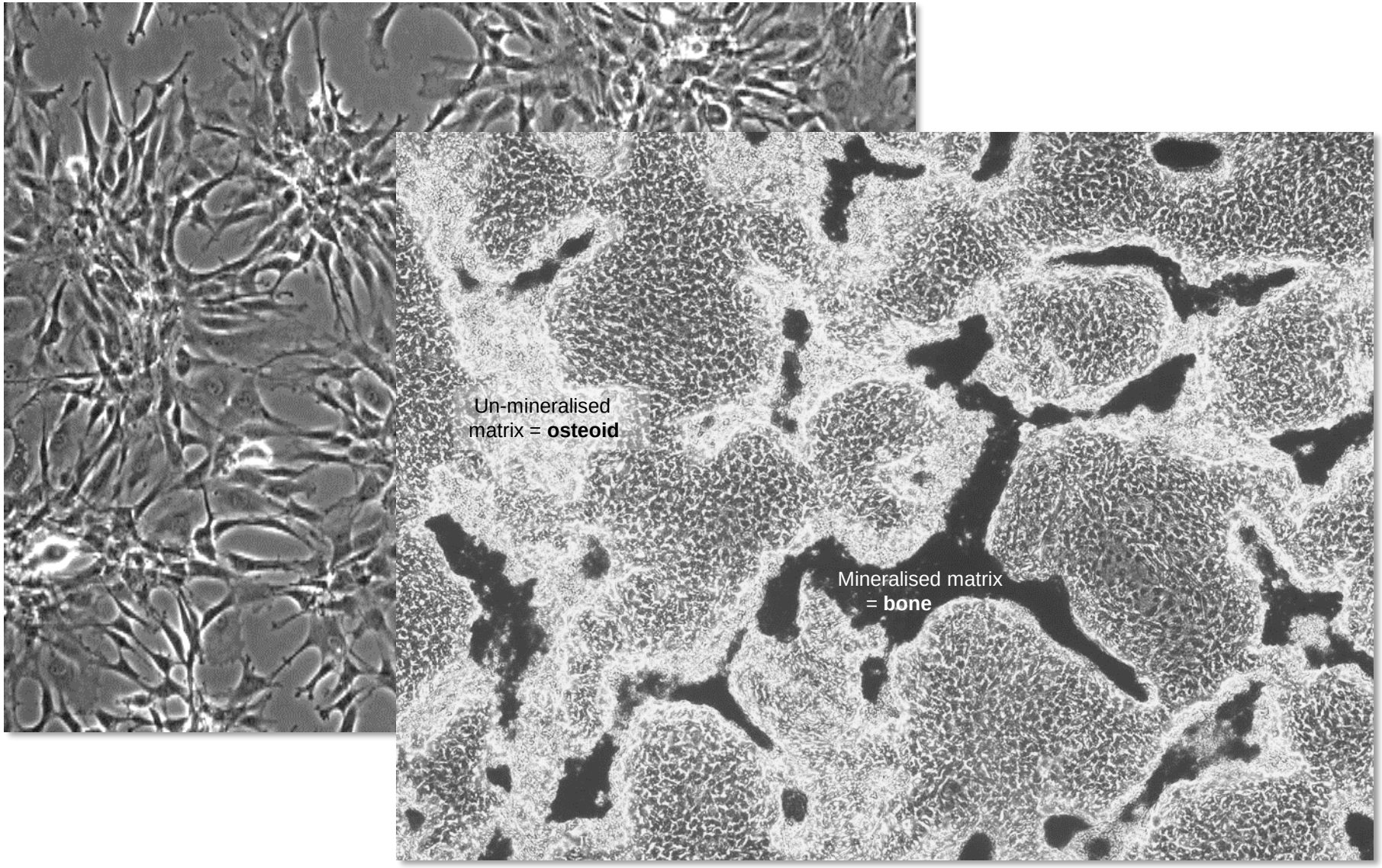
Rapid formation of ‘woven’ bone (jaw) in developing embryo



‘Woven’ bone – *rapid turnover*



Osteoblasts self-organise to form bone in culture



Two types of bone

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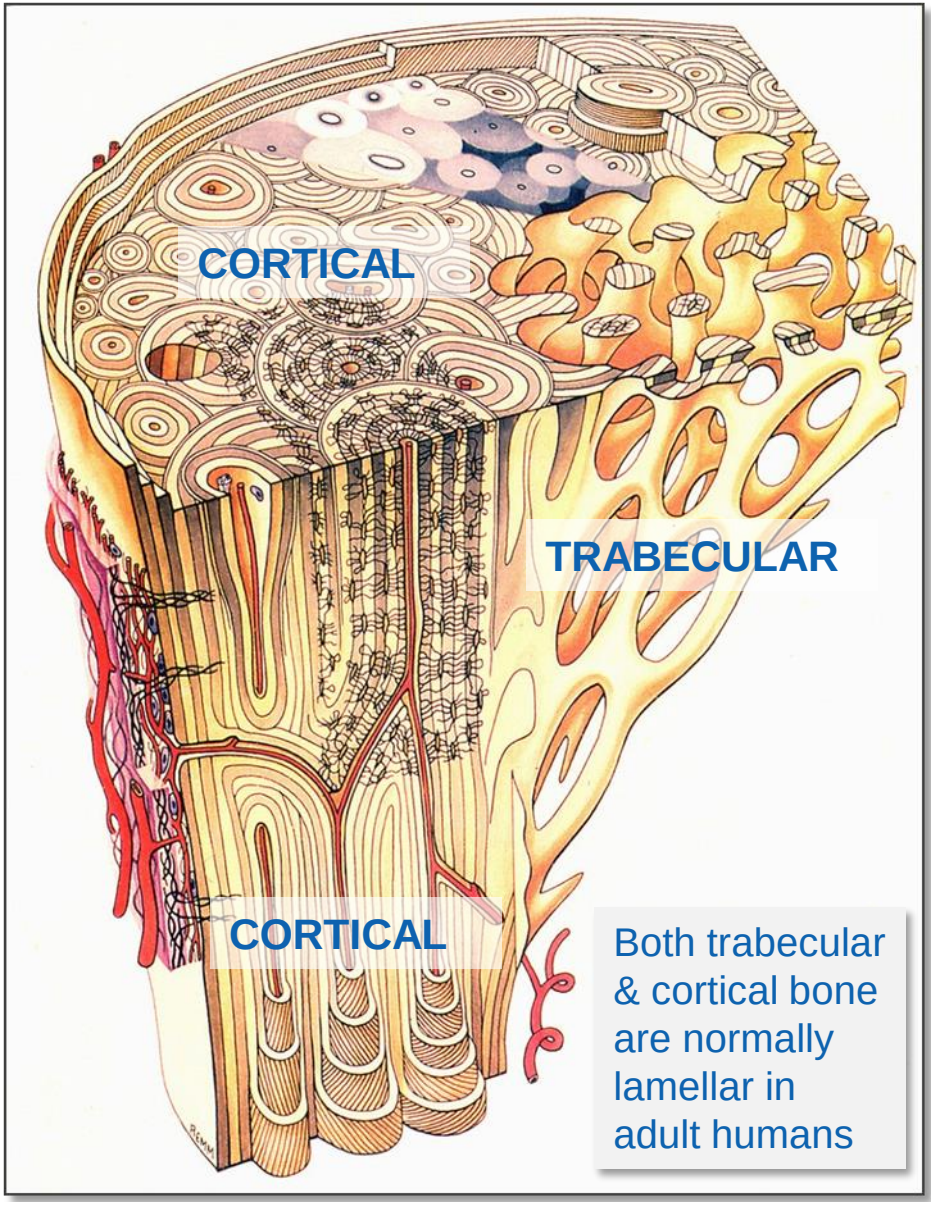
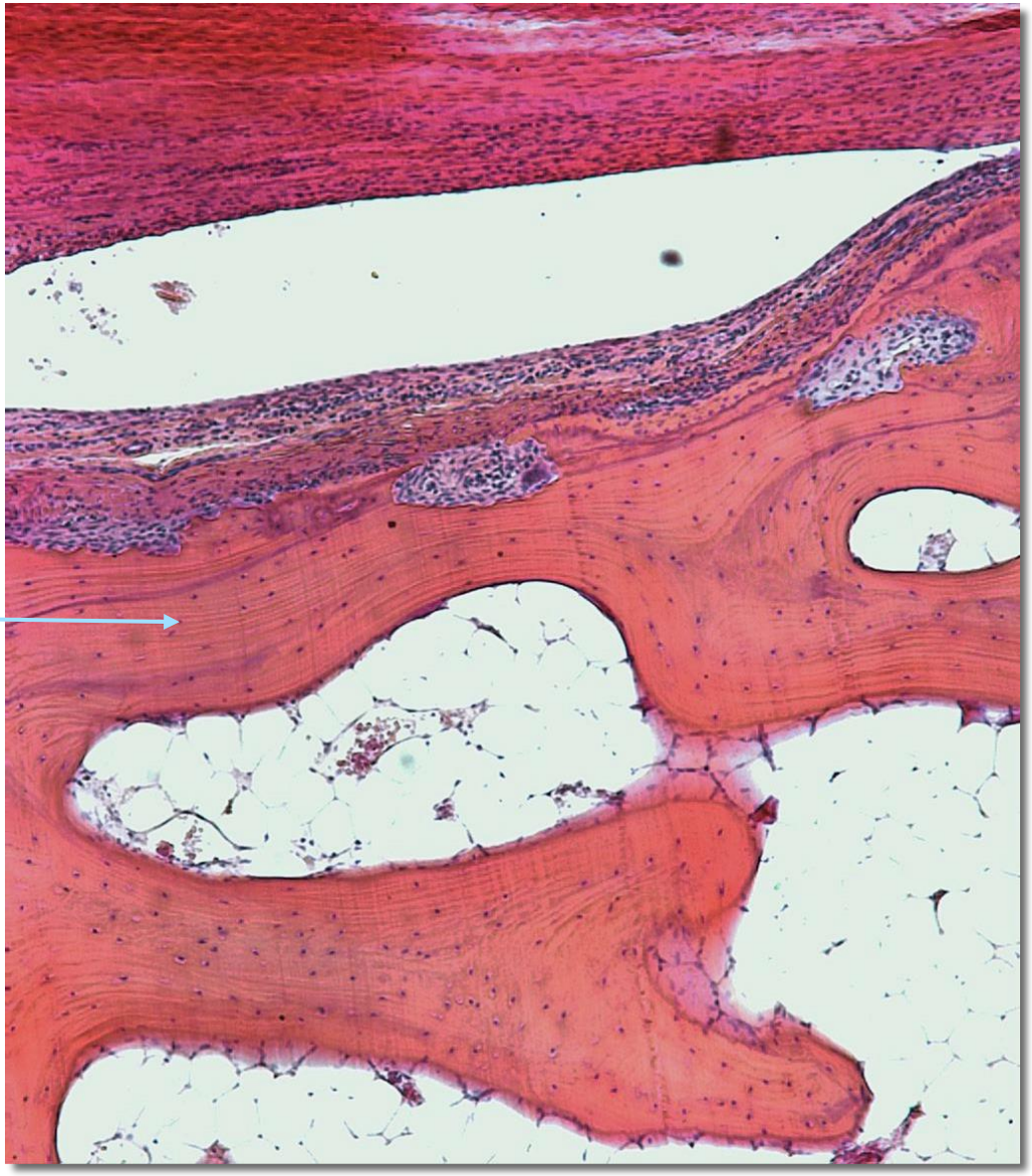
Lamellar bone (adult, mature)

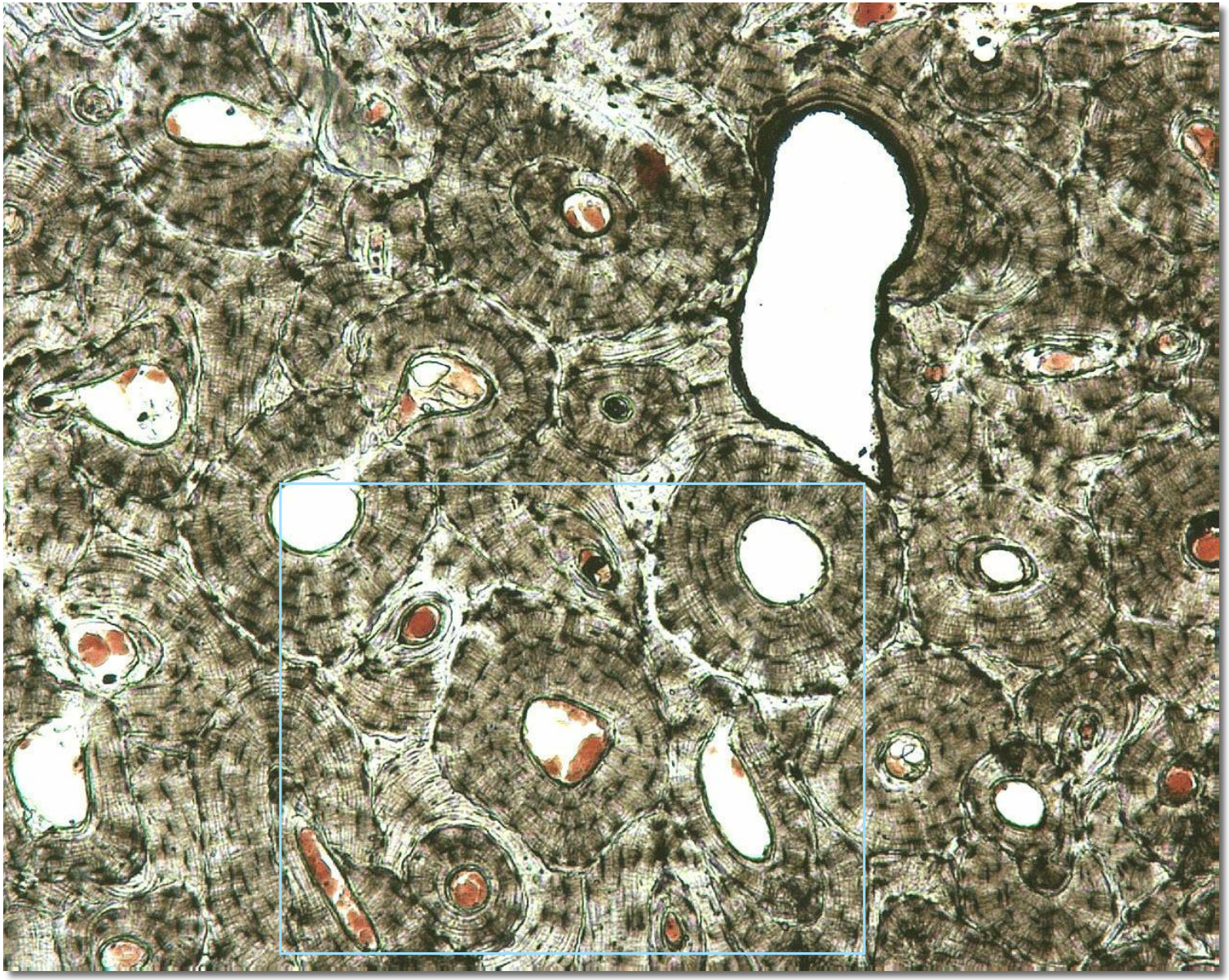


Both trabecular & cortical bone are normally lamellar in adult humans

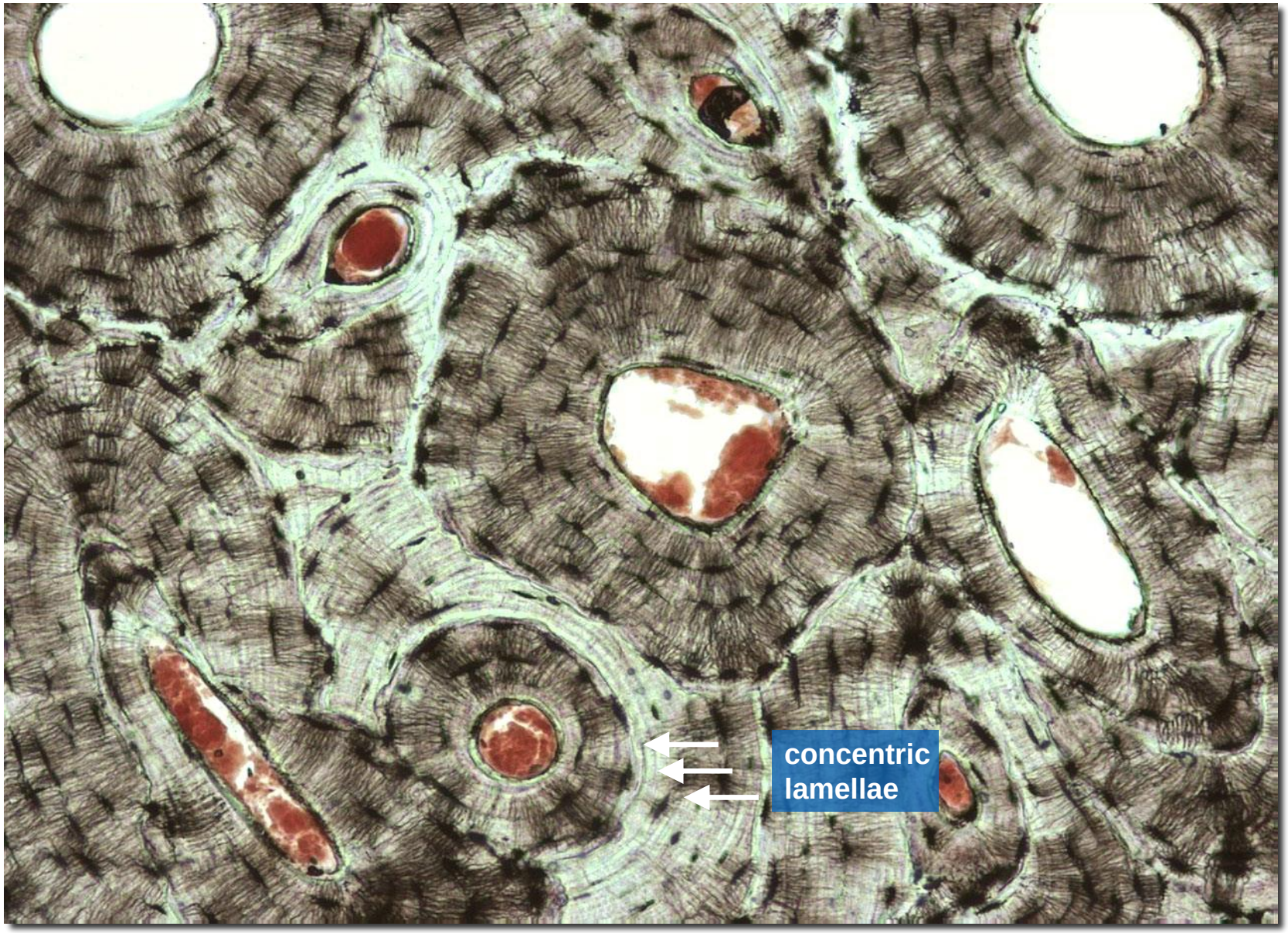
Lamellar bone - *phalanx*



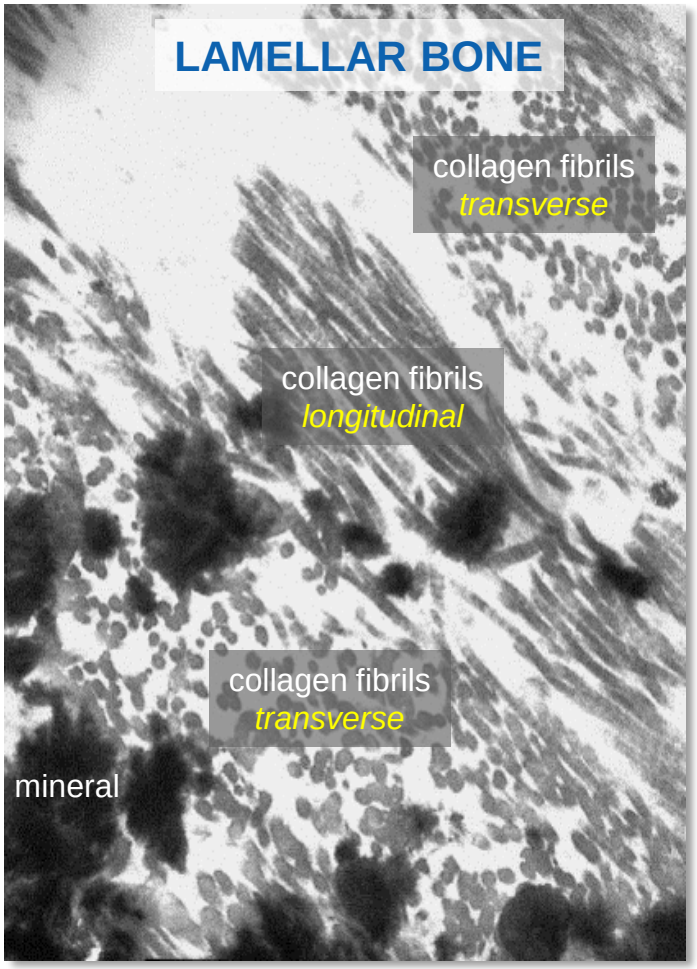
Osteonal (Haversian) systems in human cortical bone



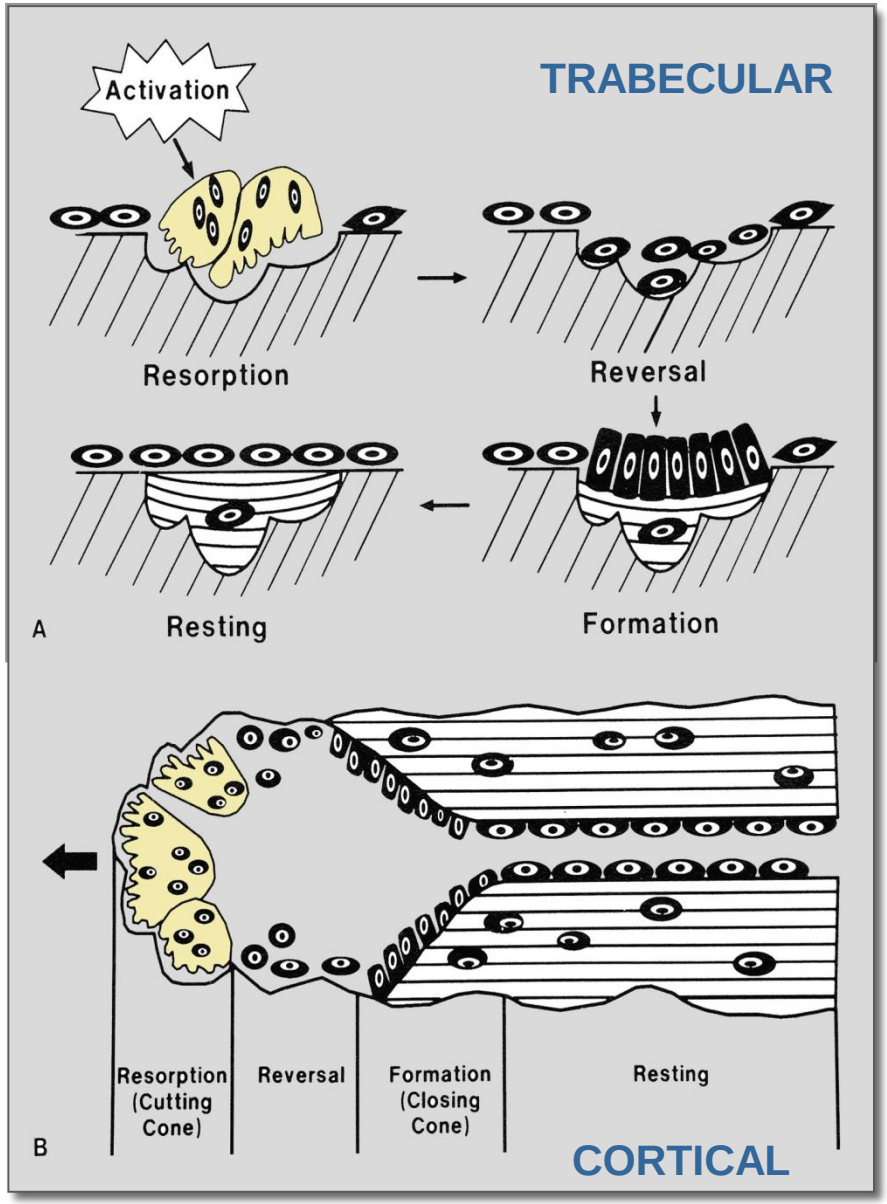
Lamellar structure of human cortical bone (osteonal / Haversian systems)

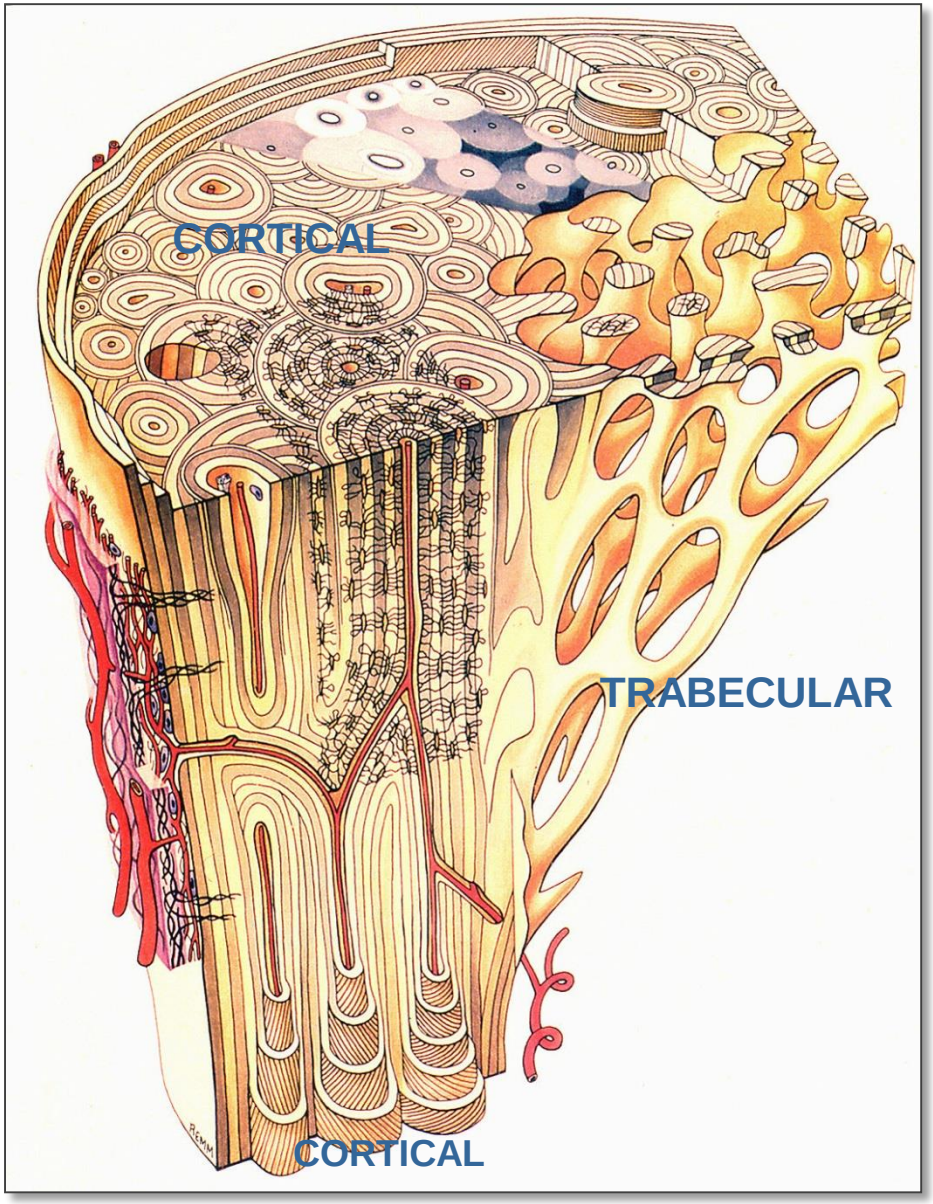


Transmission electron micrographs of woven and lamellar bone



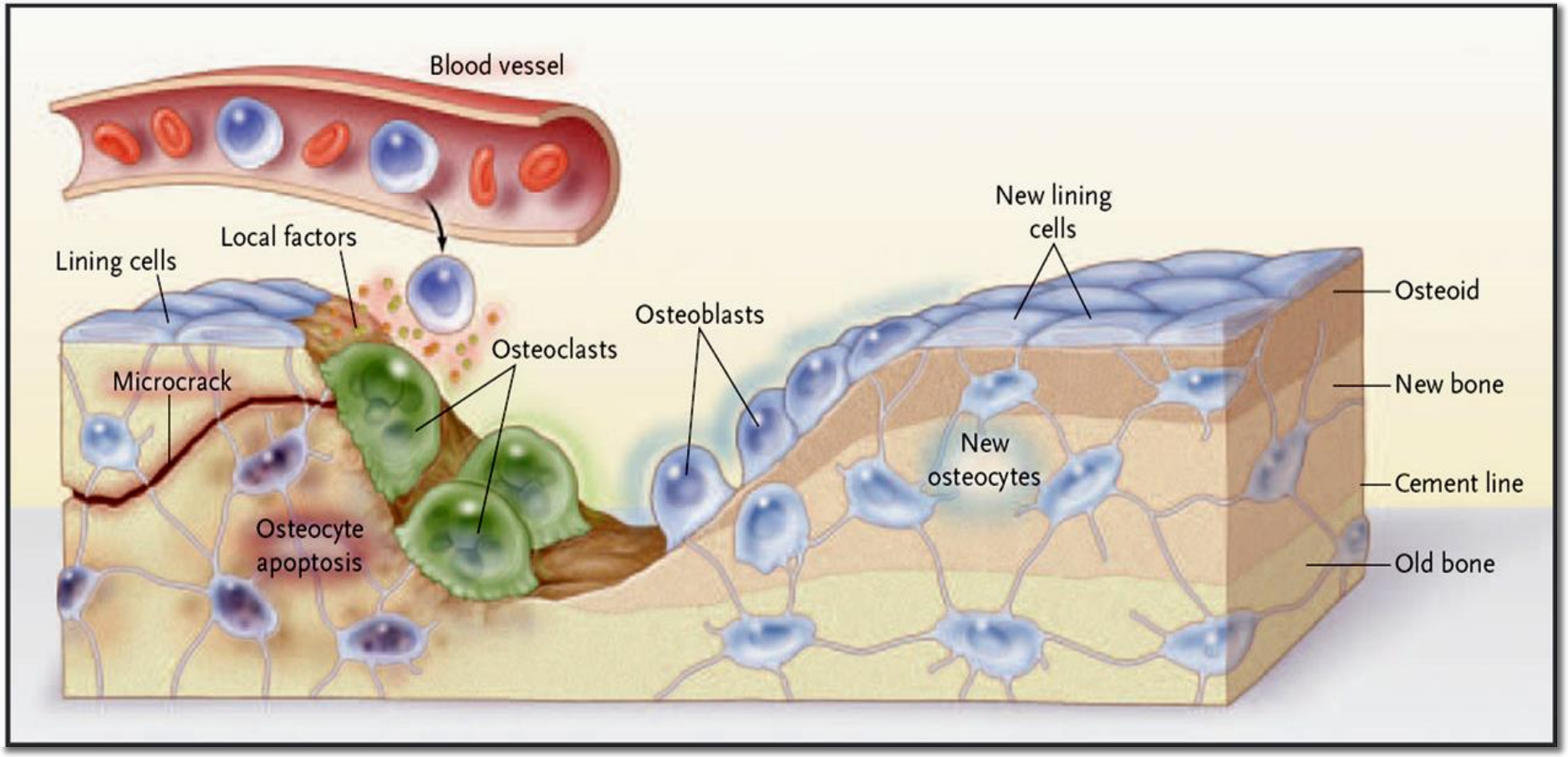
Remodelling in trabecular and cortical bone





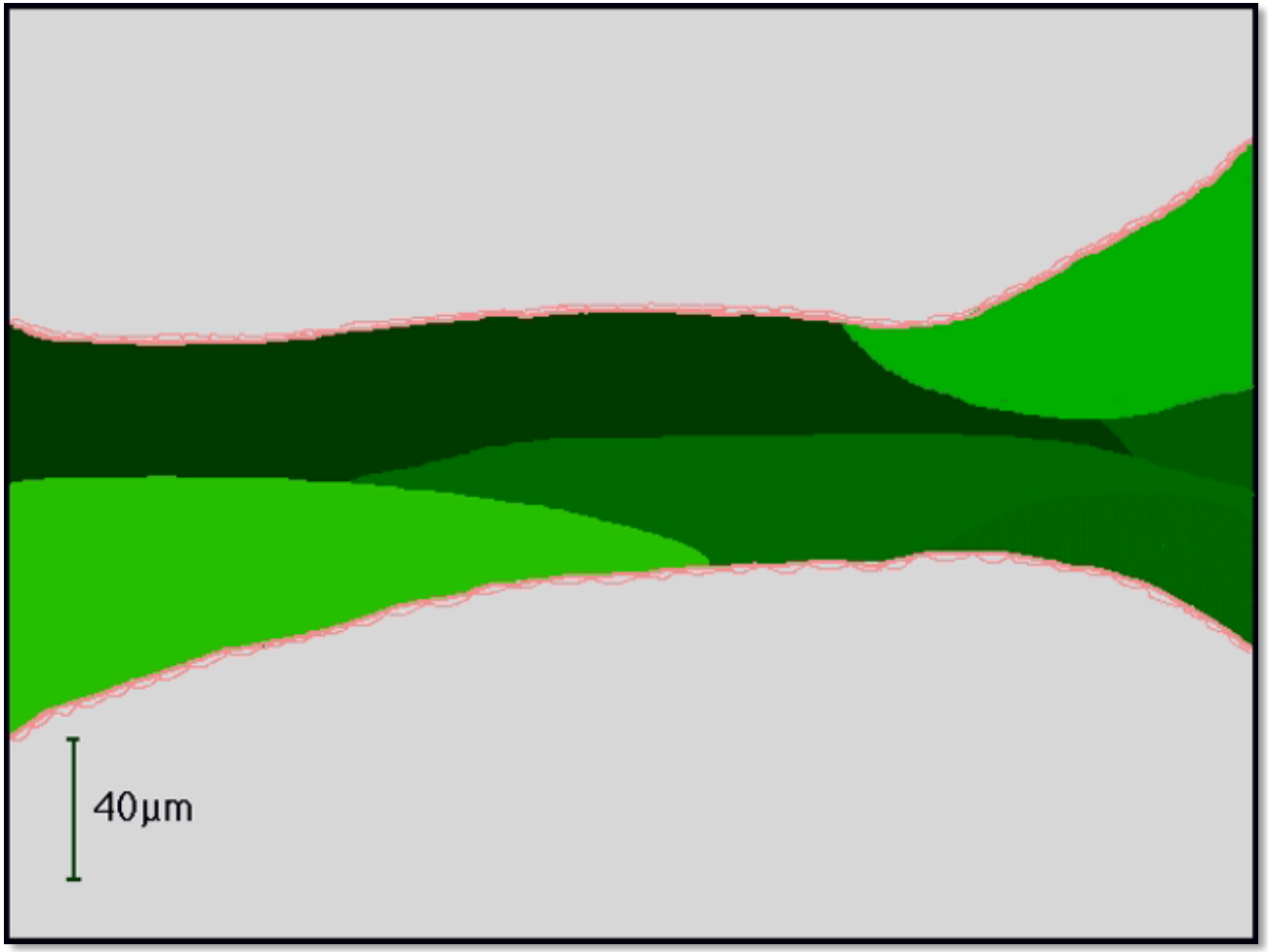
Bone surface remodelling

on a peri/endosteal surface or trabecular element



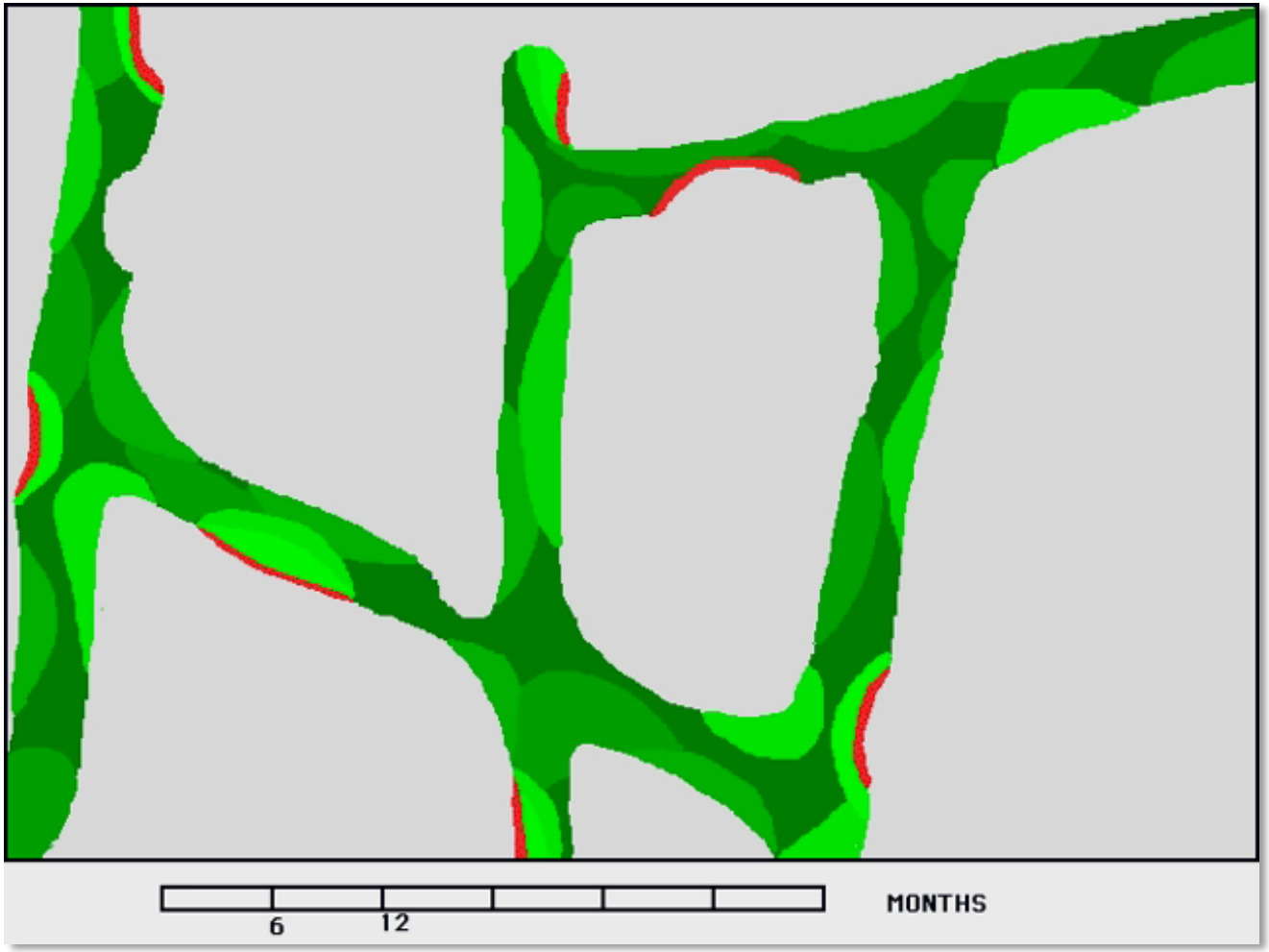
Normal turnover

- single trabeculum



See - http://courses.washington.edu/bonephys/
(Osteoporosis & Bone Physiology, Dr Susan Ott, University of Washington)

Normal turnover in trabecular bone



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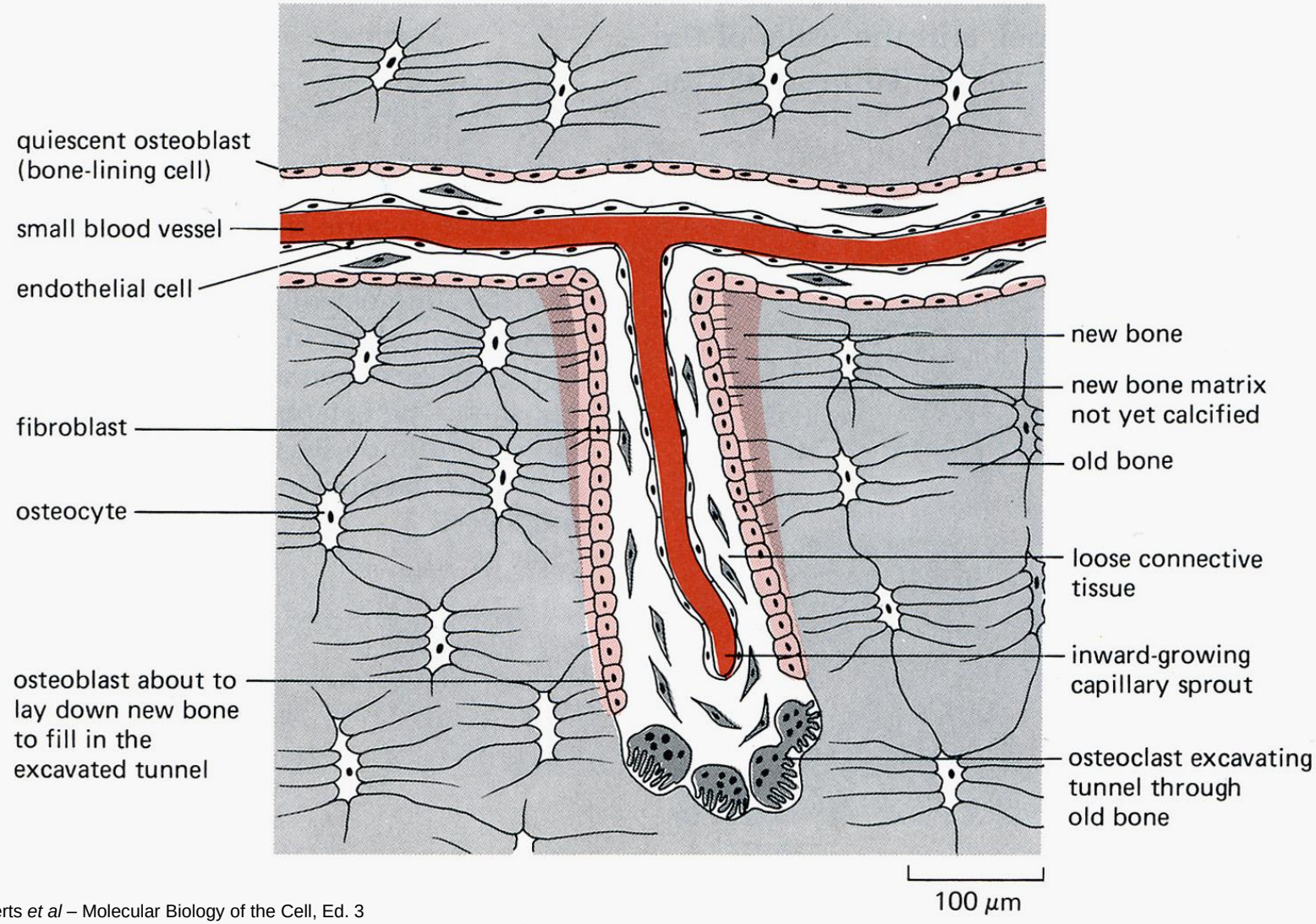
Remodelling in cortical bone
- *tunelling*

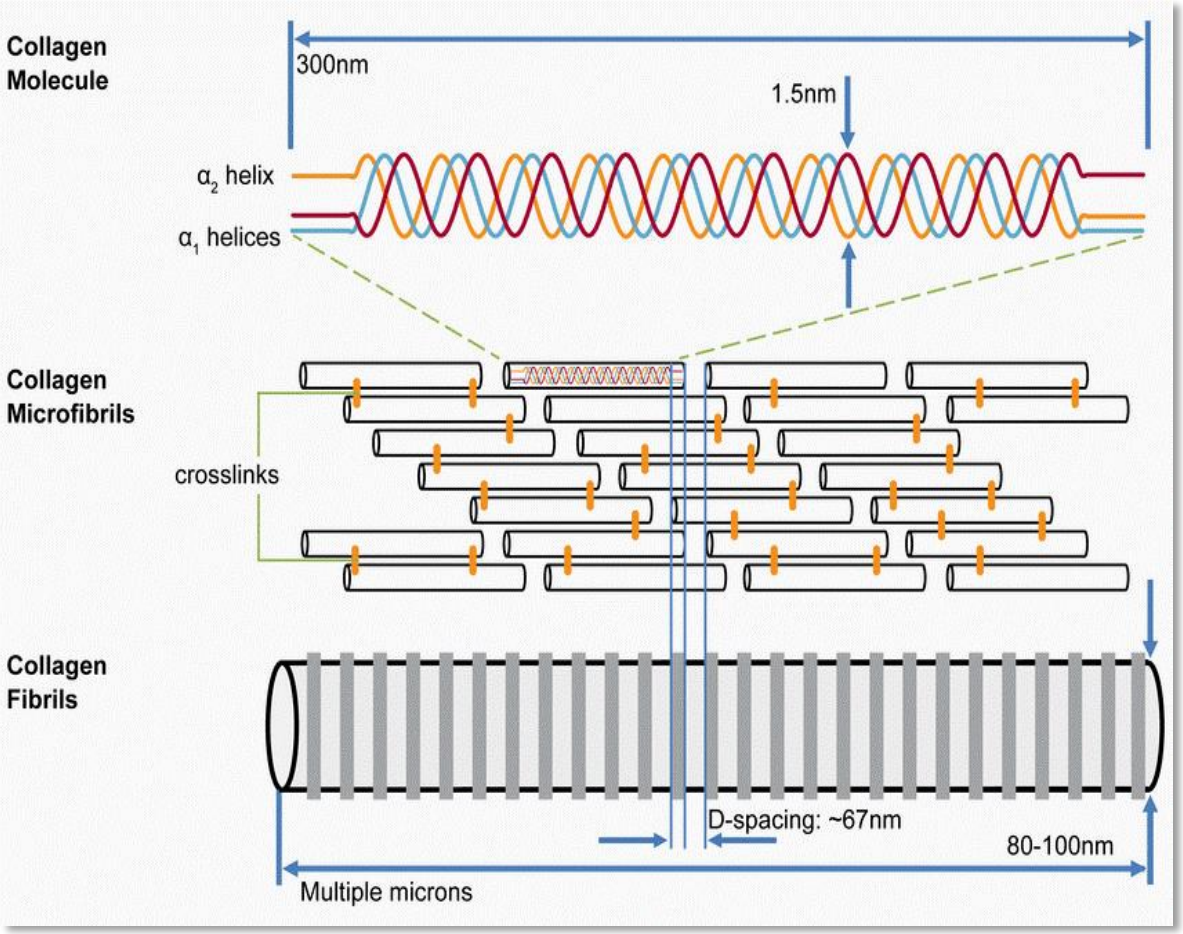


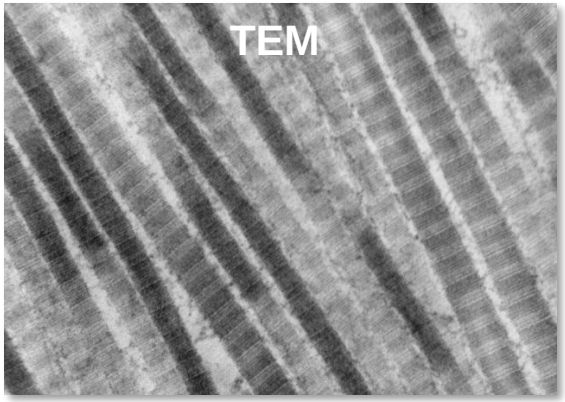
Alberts *et al* – Molecular Biology of the Cell, Ed. 3

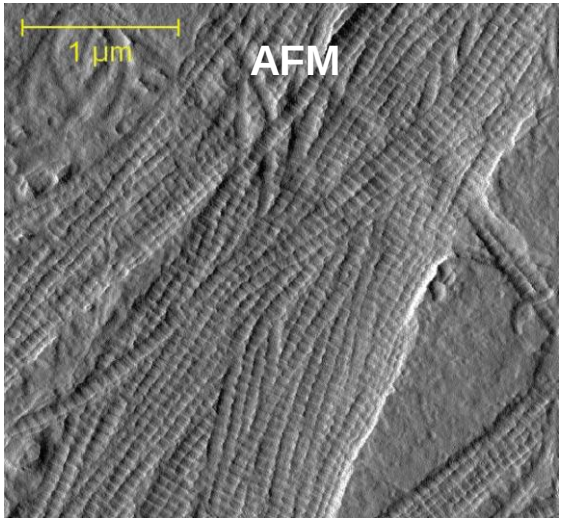
Bone turnover rates

- Adult human cortical (compact) bone replaced every ~15 years
- Turnover rate in trabecular (cancellous) bone is ~10 x greater because of high surface area
- Bone destruction by osteoclasts is much faster than bone formation by osteoblasts
- ⇒ Effects of remodelling imbalances appear sooner in skeletal sites with a high proportion of trabecular bone (*eg* - vertebral bodies)

Collagen structure

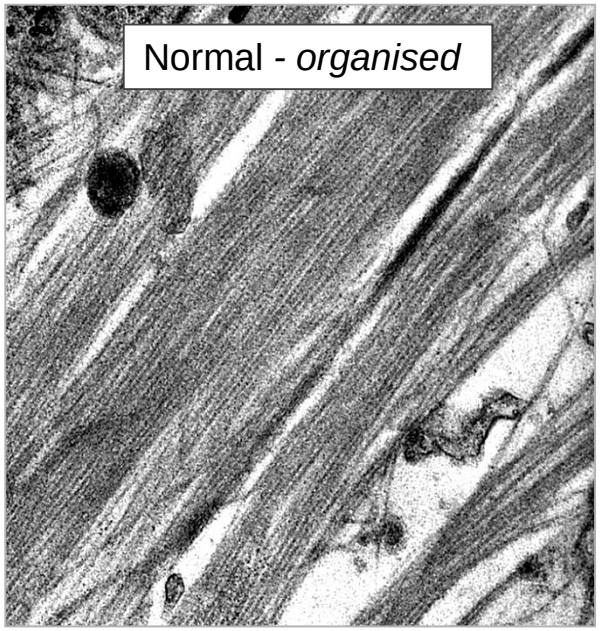


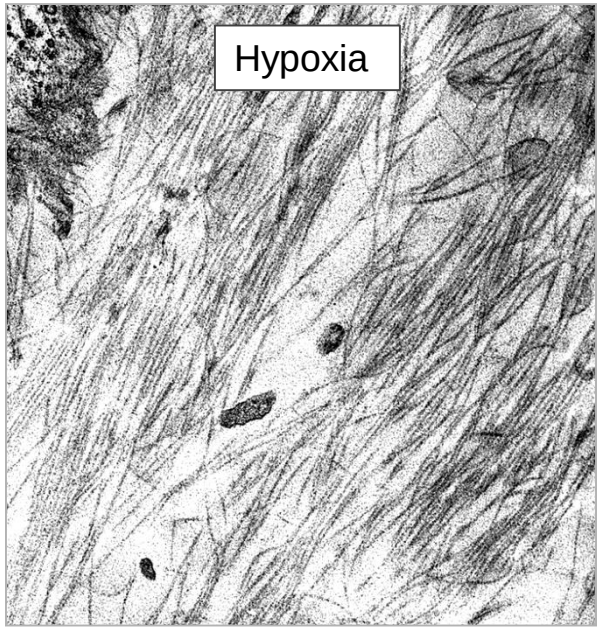




Canelon & Wallace *PLoS One* (2016)

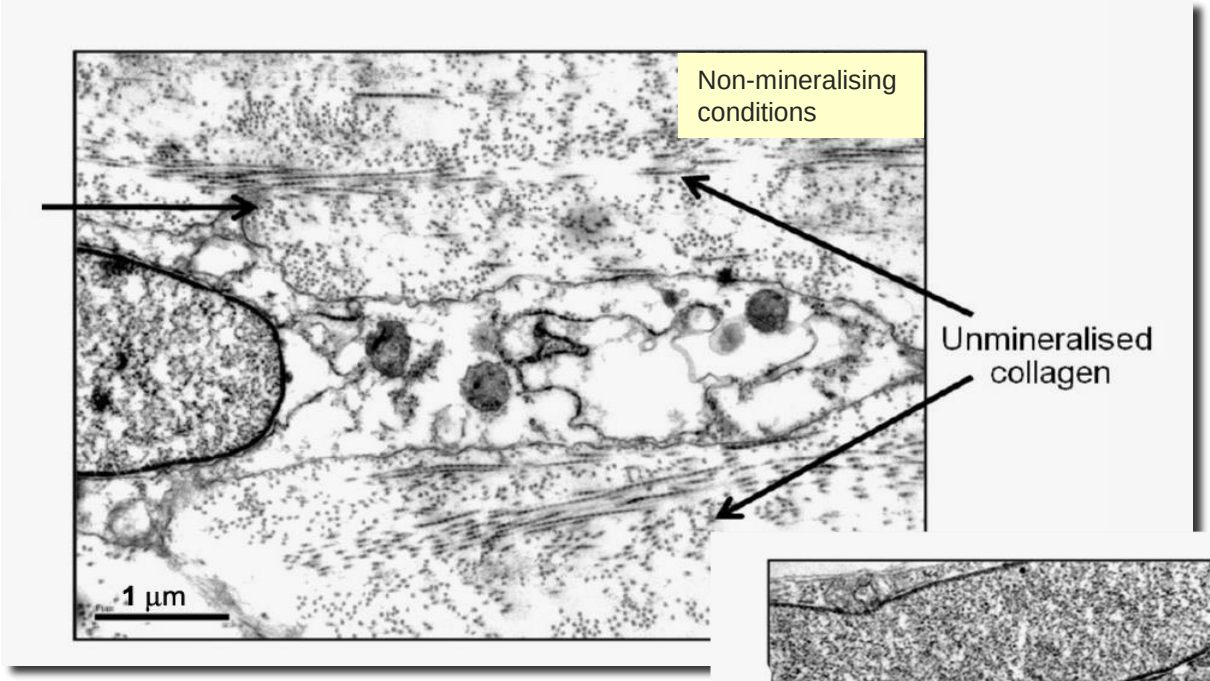
Type 1 collagen fibrils formed by cultured osteoblasts



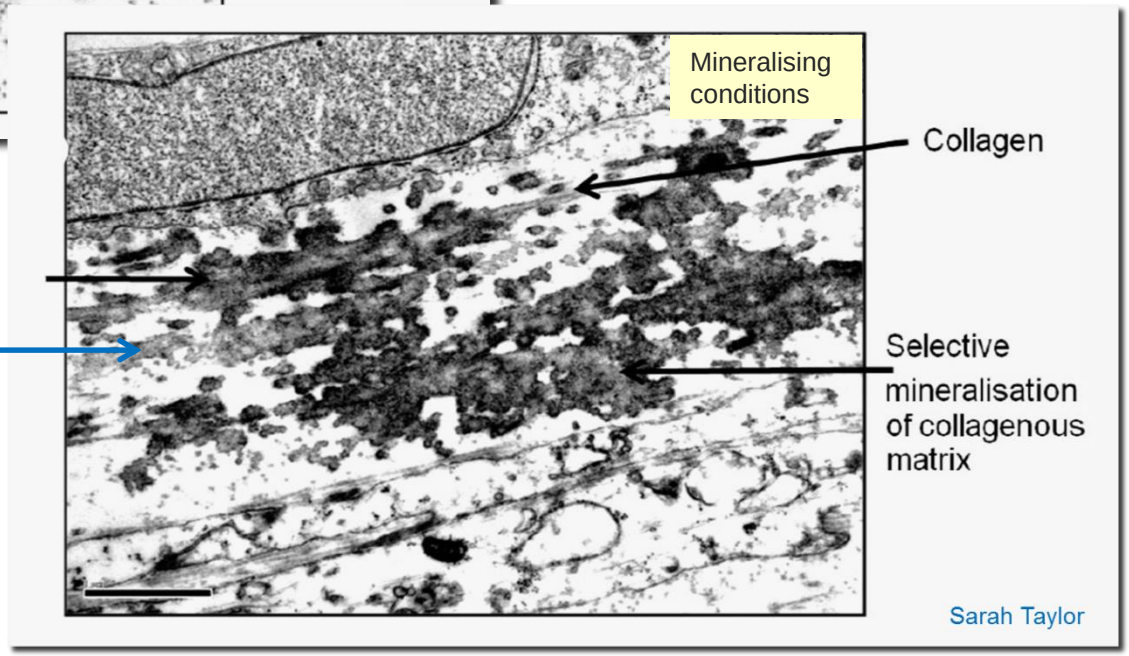


Collagen synthesis is highly oxygen-dependent

Selective mineralisation of type 1 collagen fibres laid down by cultured rat osteoblasts



Transmission electron micrographs

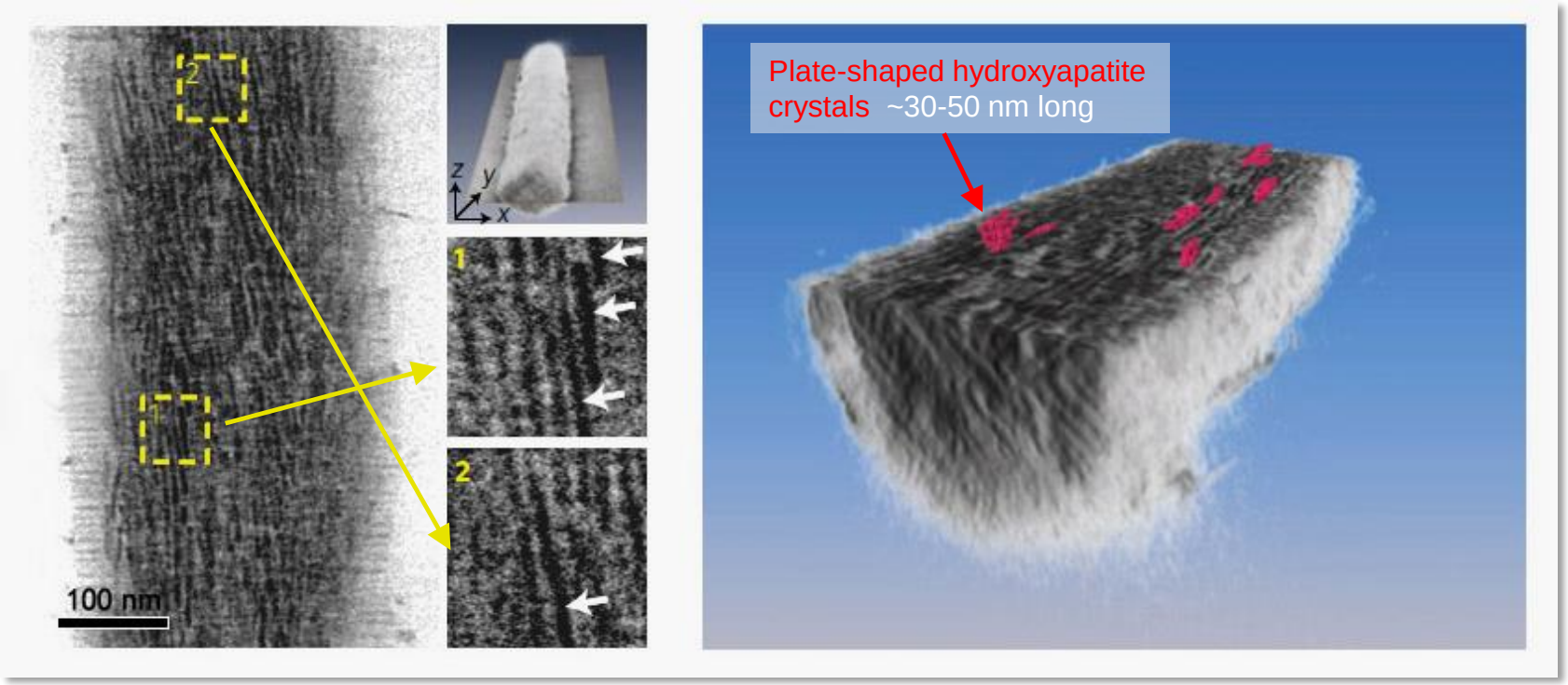


mineralisation confined to extracellular matrix

cells not mineralised

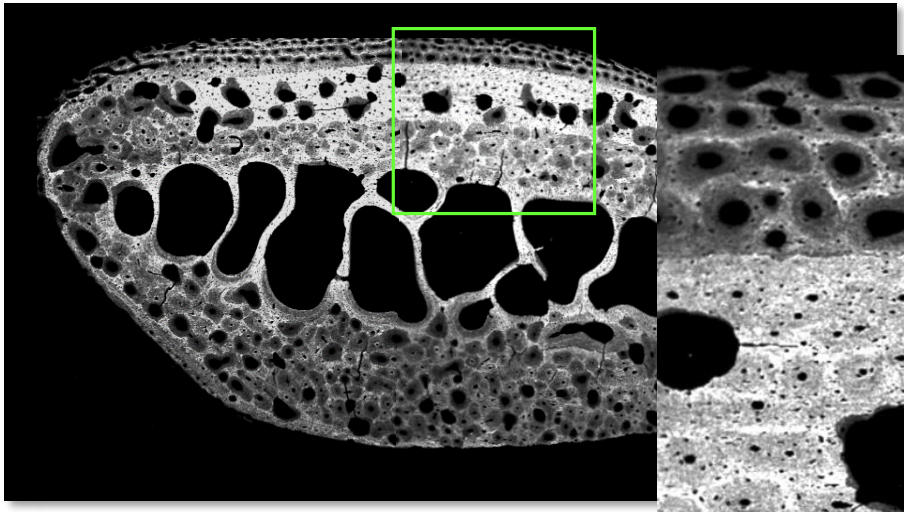
Mineralisation of a single collagen fibril

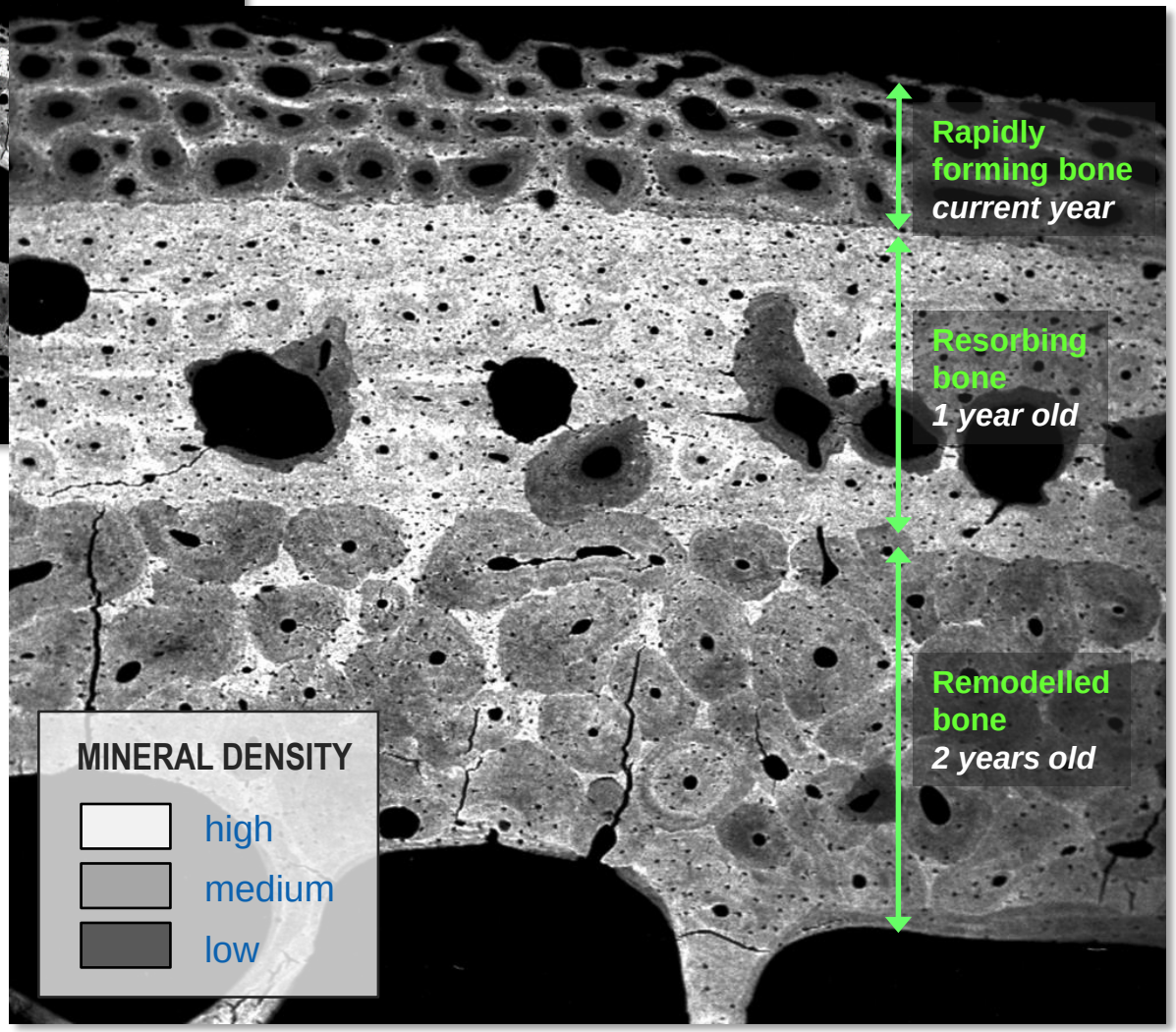
Imaged by 3-D transmission electron microscopy



Nudelman F et al (2010) *Nature Materials*

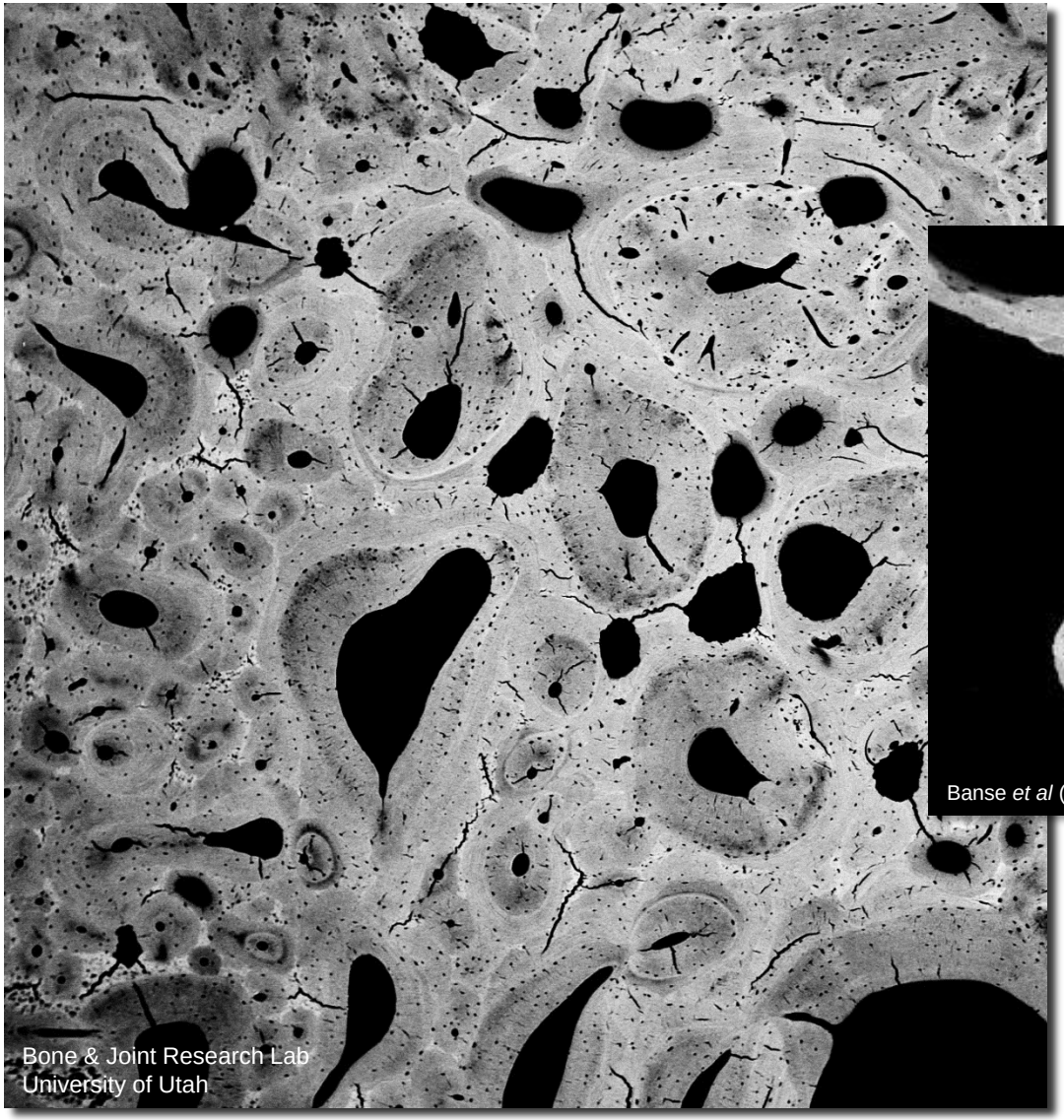
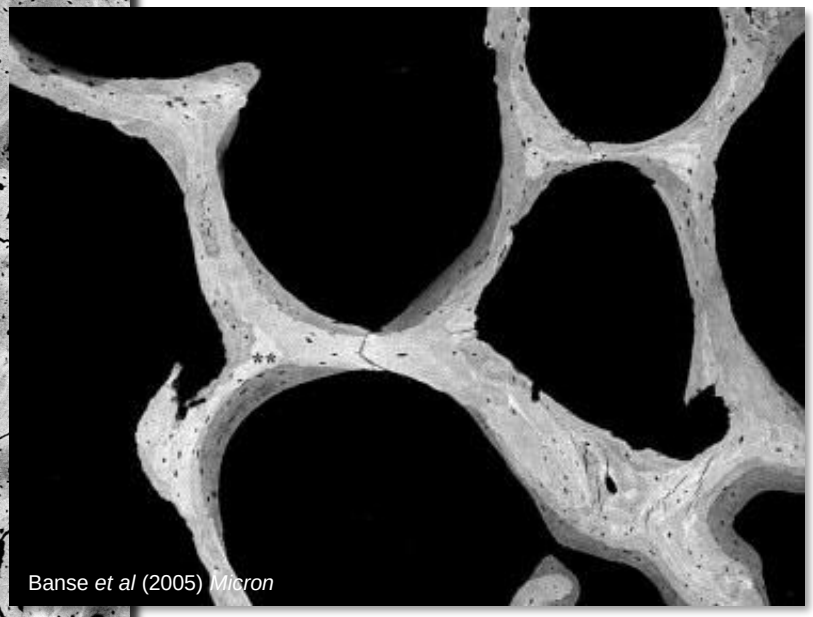
Seasonal bone remodelling and mineral heterogeneity in sheep rib





Scanning electron microscopy
Back-scattered electron imaging

Alan Boyde - QMUL

Secondary mineralisation

Backscattered electron SEM imaging - old bone more highly mineralised - reflects electrons (*appears white*)