Biomechanics and mechanobiology of bone

Tim Skerry

University of Sheffield UK

Biomechanics: the mechanics of living organisms

- Forces acting on tissues
- Material properties
- Consequences on tissue function
- Consequences on tissue response

What do bones do?

Bones protect the vital soft organs
– brain, heart, lungs etc

Bones allow muscles to work
to move us around

Bones store mineral

Only the mechanical functions
account for shape and structure

What makes a strong bone - one resistant to fracture?

- What is bone made of?
- Why does it matter?
- What are the consequences of different compositions
- What do we need to have a fracture resistant bone in life?

Composite materials

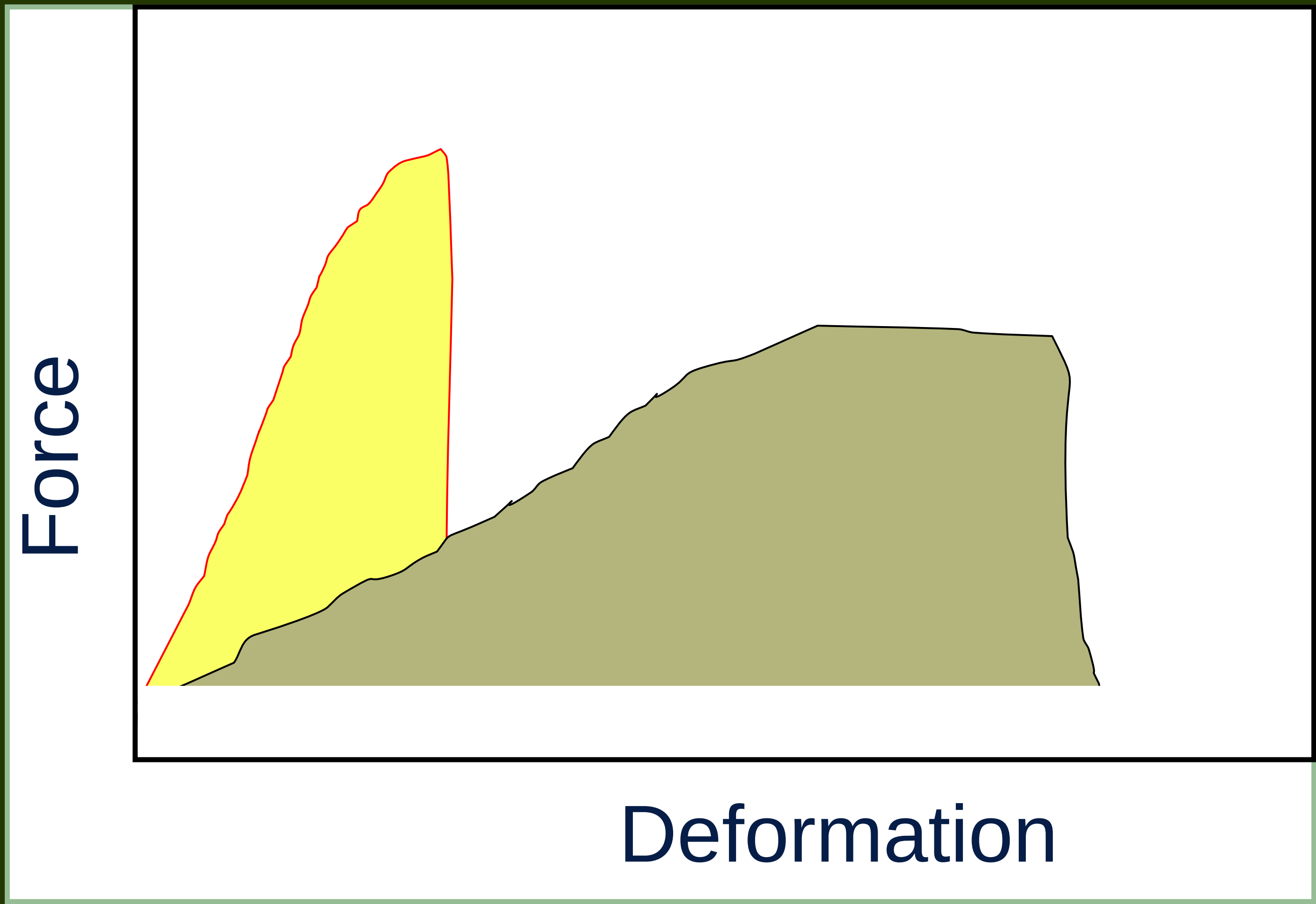
- Contain materials with
  - Compressive strength
  - Tensile strength

- Strength >> sum of the parts

Bone as a composite

- Collagen/mineral ratios differ
- Some bones are compliant
- Some are very stiff

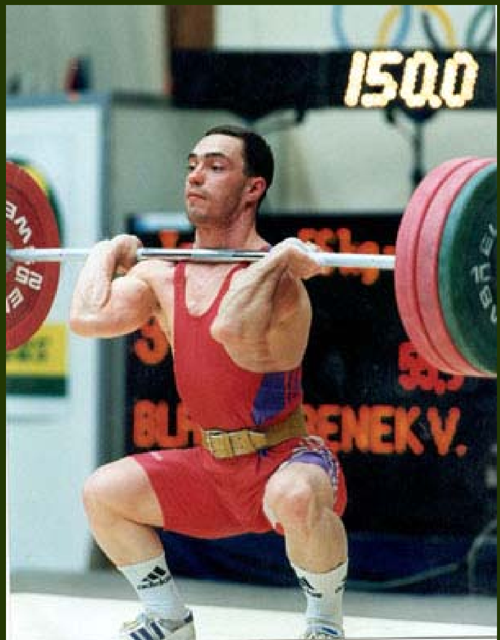
Stiff and Tough are not the same

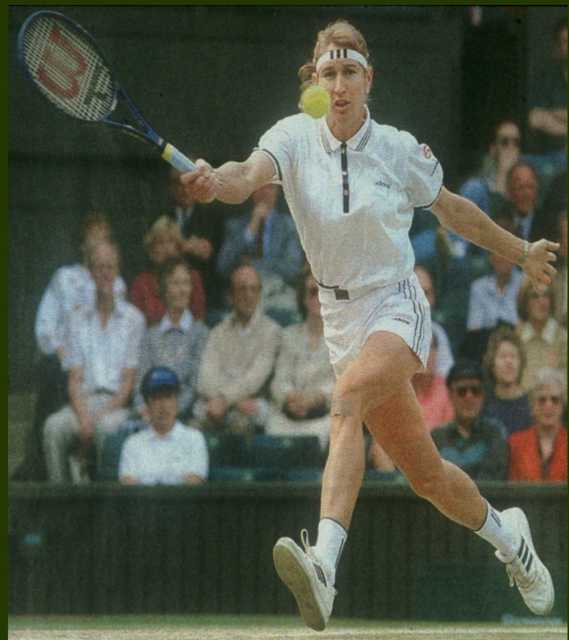


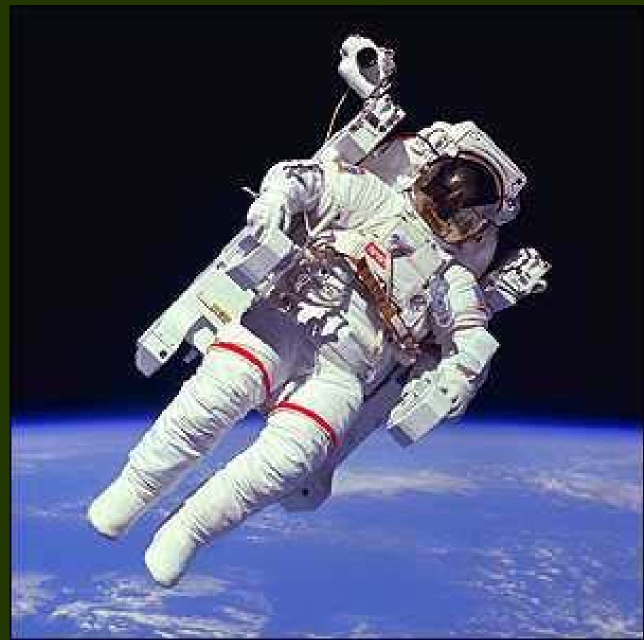
Biomechanics: the mechanics of living organisms

- Forces acting on tissues
- Material properties
- Consequences on tissue function
- Consequences on tissue response

Different individuals have different skeletal requirements



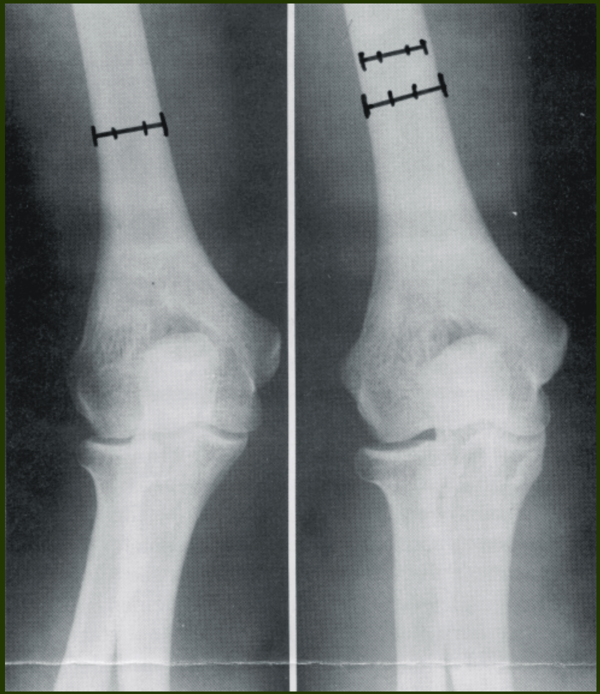




HUMERAL HYPERTROPHY IN RESPONSE TO EXERCISE

BY
HENRY H. JONES, M.D., JAMES D. PRIEST, M.D., WILSON C.HAYES, PH.D.,
CAROL CHINN TICHENOR, M.A. AND DONALD A. NAGEL, M.D.
STANFORD CALIFORNIA

J Bone Joint Surg 59A 204-208 1977

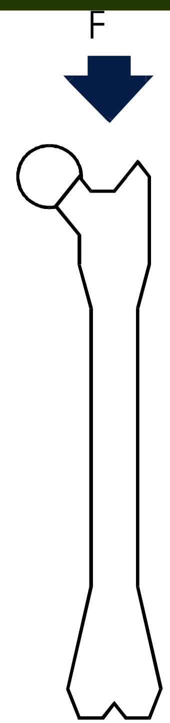


- What happens to bones when they are loaded?

Deformation

Force (F) causes deformation (δL)

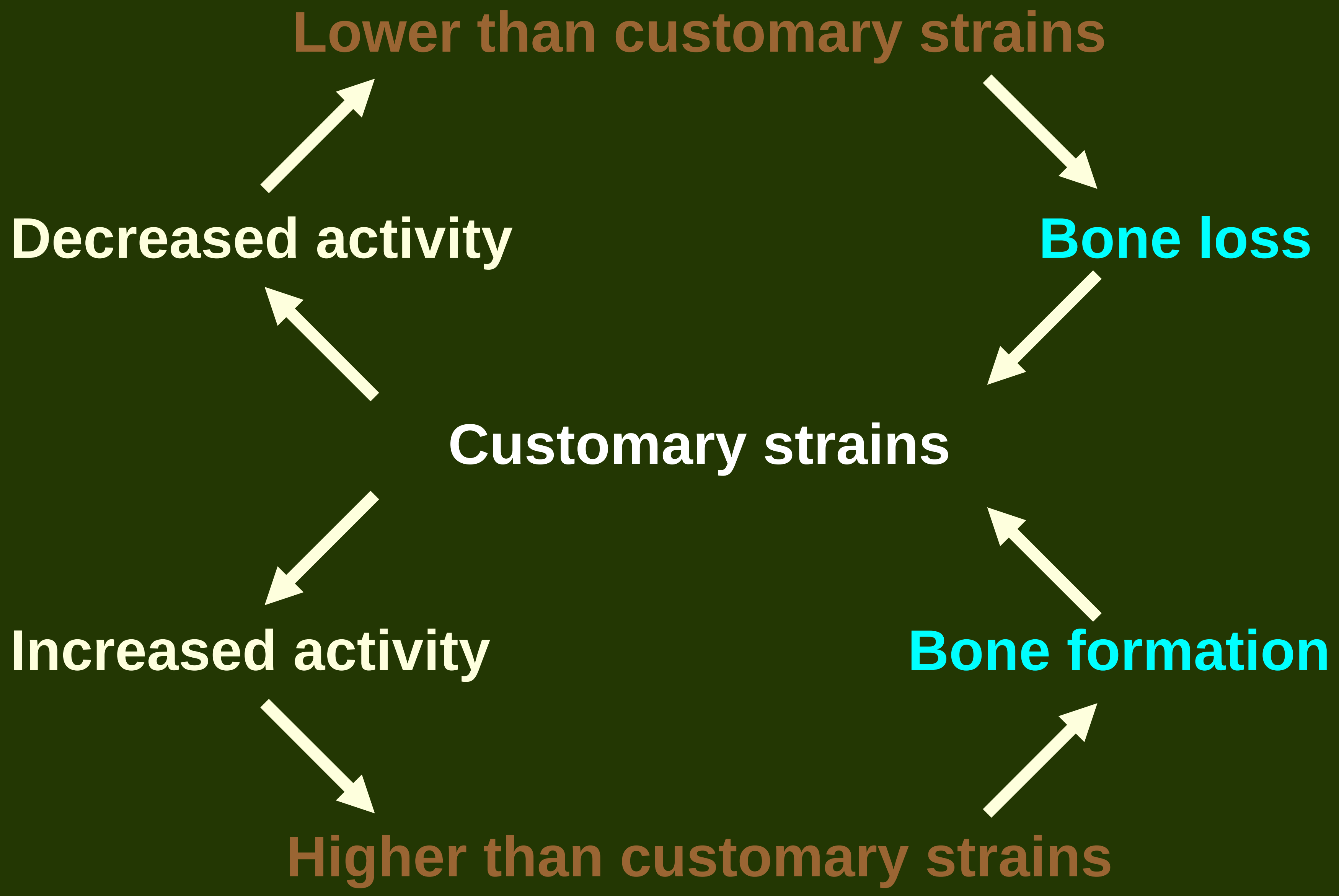
Strain =δL/L



Femur: 600mm
Deformation =0.6mm
Strain =0.6/600=0.1%

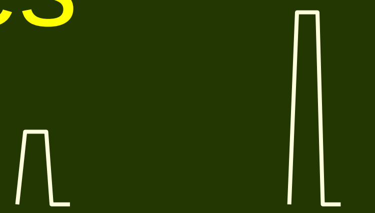
Peak bone strains different species

Activity	Strain x10,000
Galloping horse	2-3,000
Flying goose	~2,000
Flapping turkey	<2,500
Running Pig	~2,000
Running human	~2,000


Lower than customary strains
Decreased activity
Bone loss
Customary strains
Increased activity
Bone formation
Higher than customary strains

Strain variables

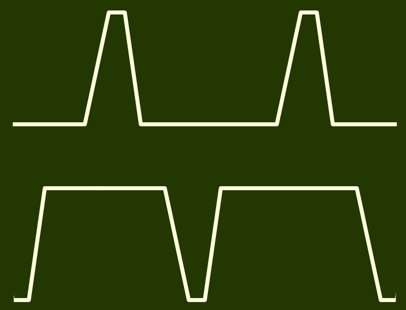
Magnitude



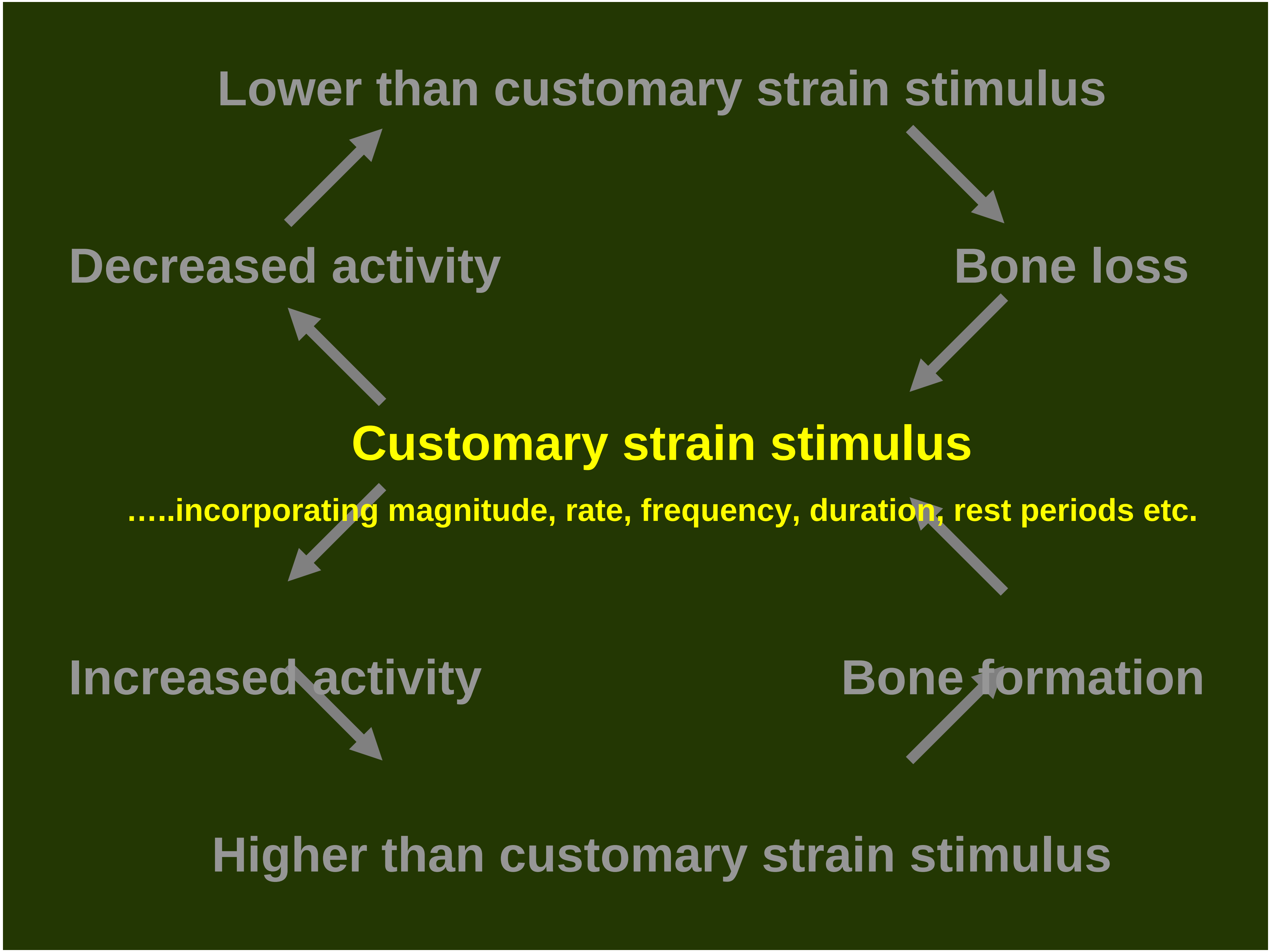
Rate (up and down)

Frequency

Dwell (hold/rest periods)



Number of cycles/duration of exercise


Lower than customary strain stimulus
Decreased activity
Bone loss
Customary strain stimulus
…..incorporating magnitude, rate, frequency, duration, rest periods etc.
Increased activity
Bone formation
Higher than customary strain stimulus

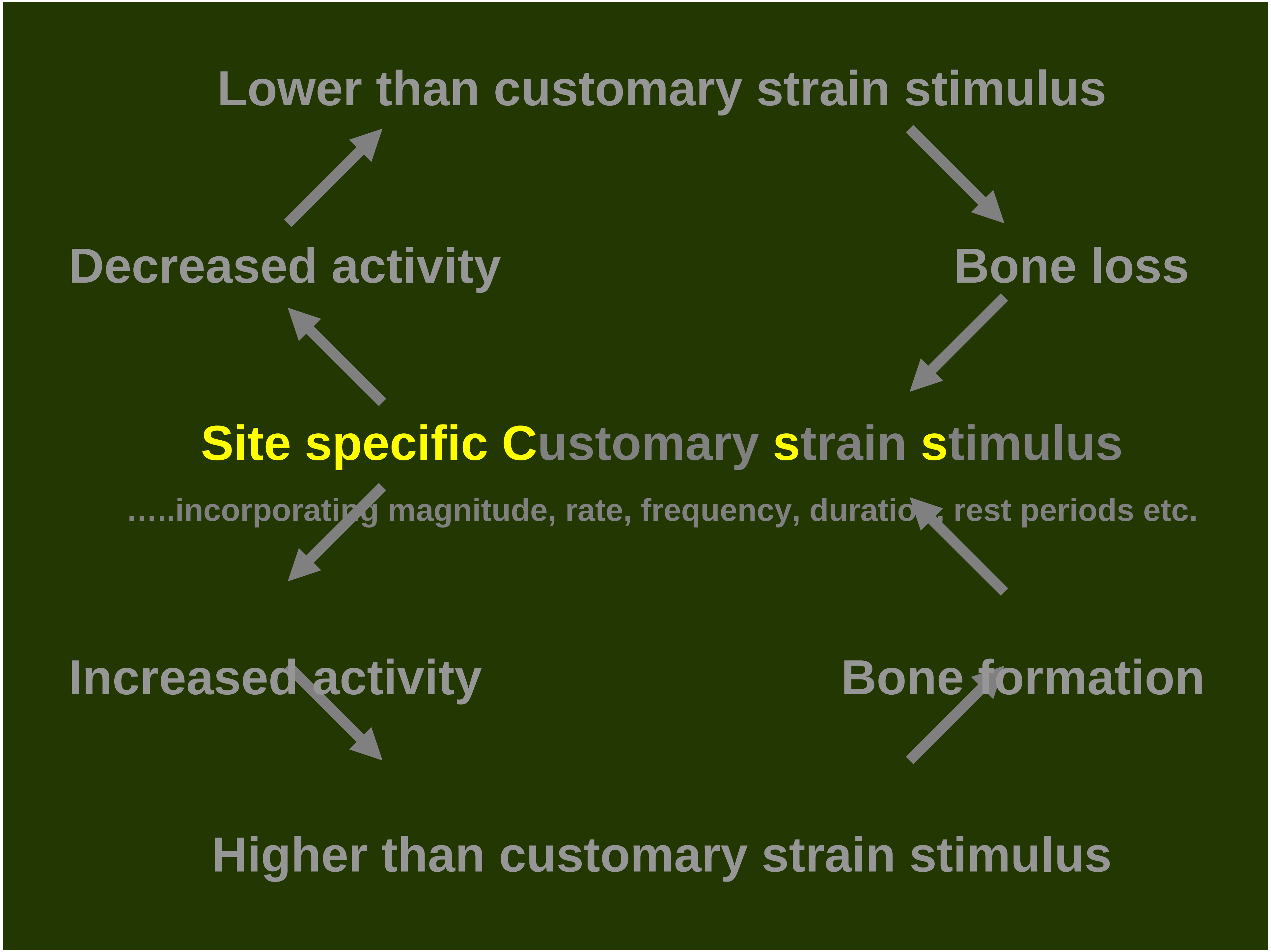
Peak bone strains different species

Activity/ Species	Strain x10,000
Galloping horse	2-3,000
Flying goose	~2,000
Flapping turkey	<2,500
Running Pig	~2,000
Running human	~2,000

Human Bone strain

Skull and tibia

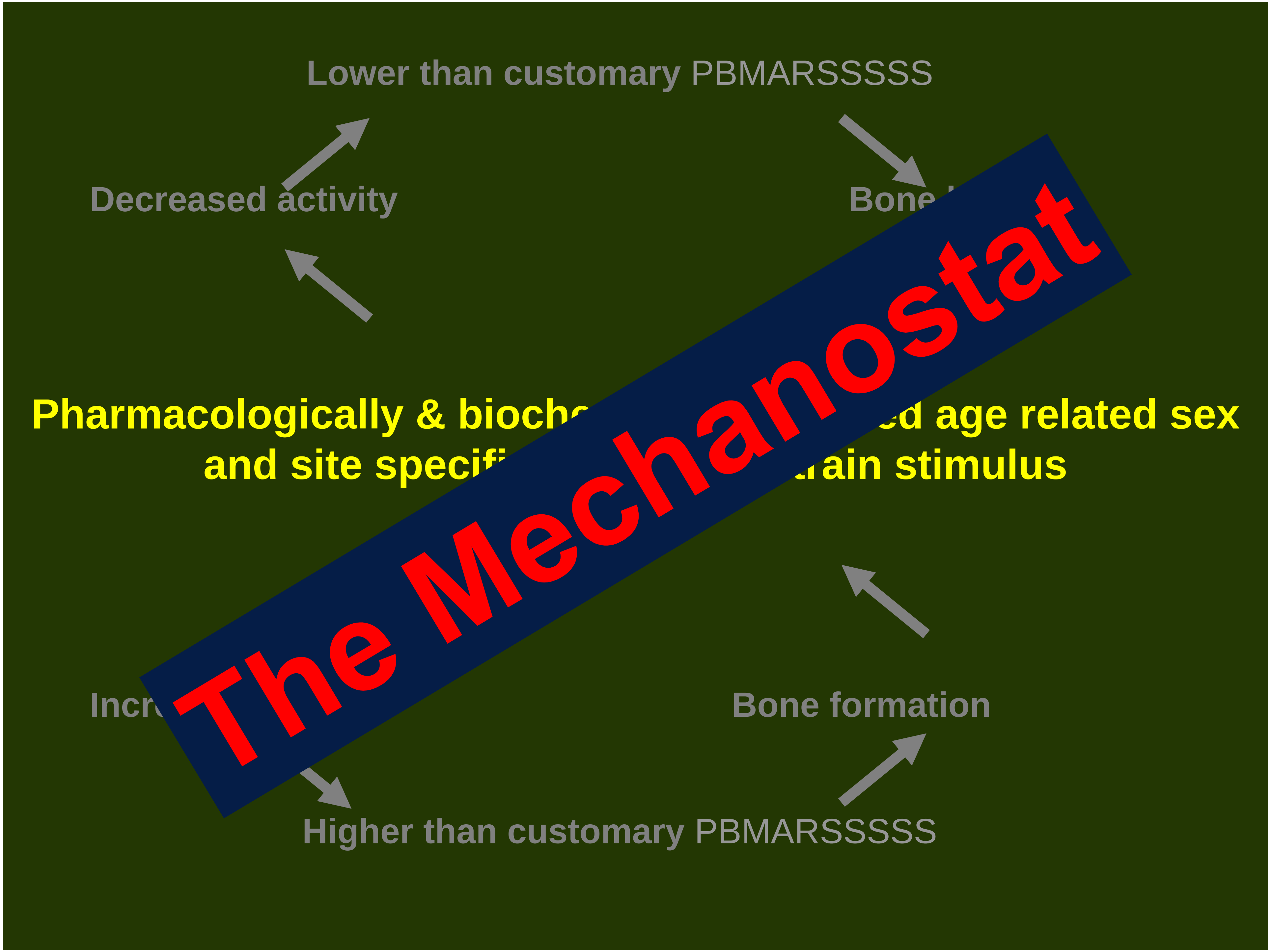
Activity	Skull Strain	Tibia x 10,000
Chewing	80	-
Smiling	100	-
Walking	50	720
Heading ball	200	840
Jump (0.45m)	170	850
Jump (1.3m)	-	2060


Lower than customary strain stimulus
Decreased activity
Bone loss
Site specific Customary strain stimulus
…..incorporating magnitude, rate, frequency, duration, rest periods etc.
Increased activity
Bone formation
Higher than customary strain stimulus

So is SSCSS the answer?

it is not that simple……

- Sex
  - SSSCSS
- Age
  - ARSSSCSS
- Biochemicals e.g Hormones, cytokines
  - BMARSSSCSS
- Drugs/medicines/nutraceuticals
  - PBMARSSSCSS


Lower than customary PBMARSSSSS
Decreased activity
Bone
Pharmacologically & bioch
ed age related sex
and site specifi
train stimulus
The Mechanostat
Incr
Bone formation
Higher than customary PBMARSSSSS

So……

- The mechanostat can sense/respond to **very** brief events
- The effect of brief events persists for ~24 hours

- Subsequent loading after a short period potentiates bone’s response to loading

- Rapid repetition of load cycles desensitises the mechanostat

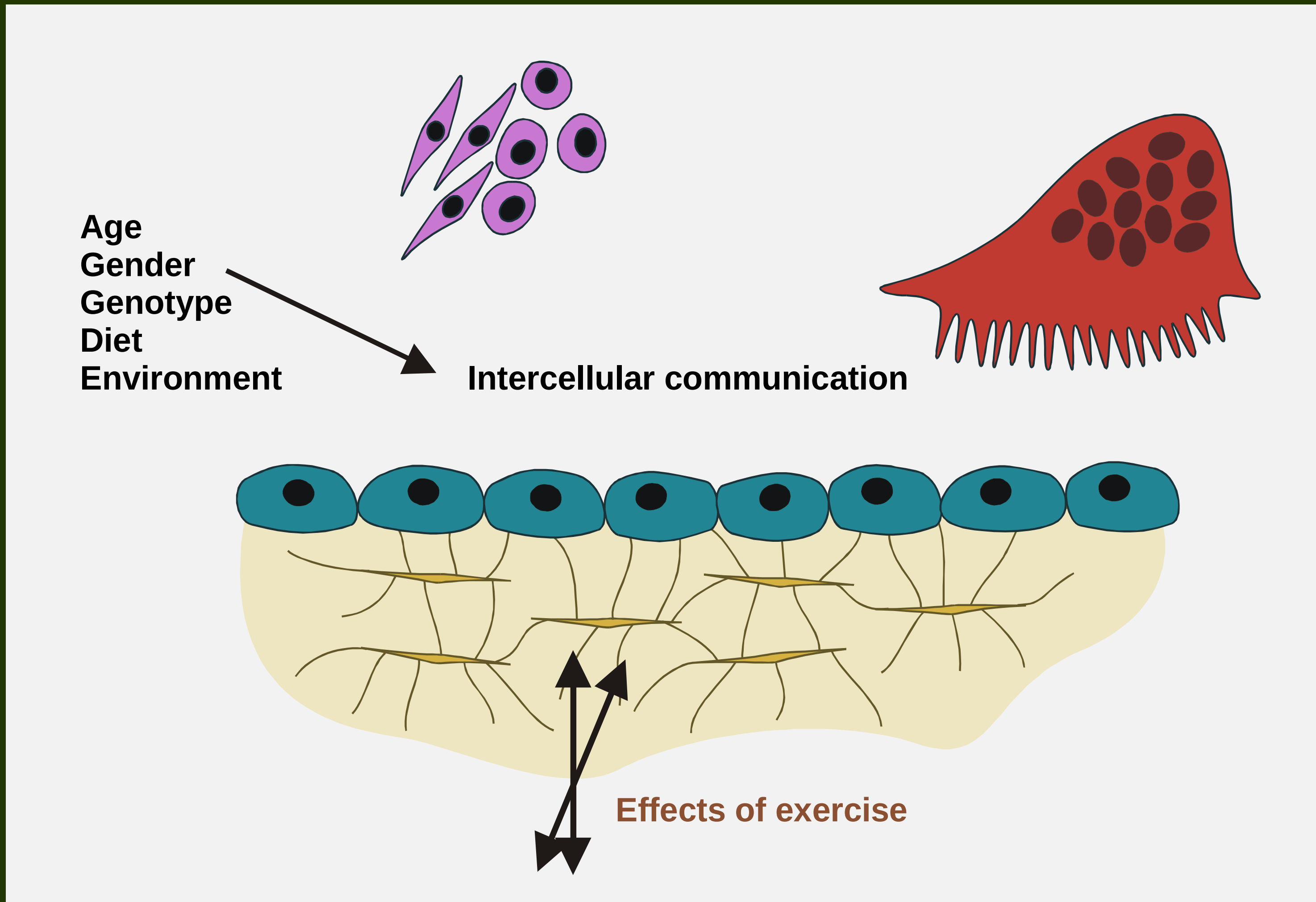
Suggesting that ..

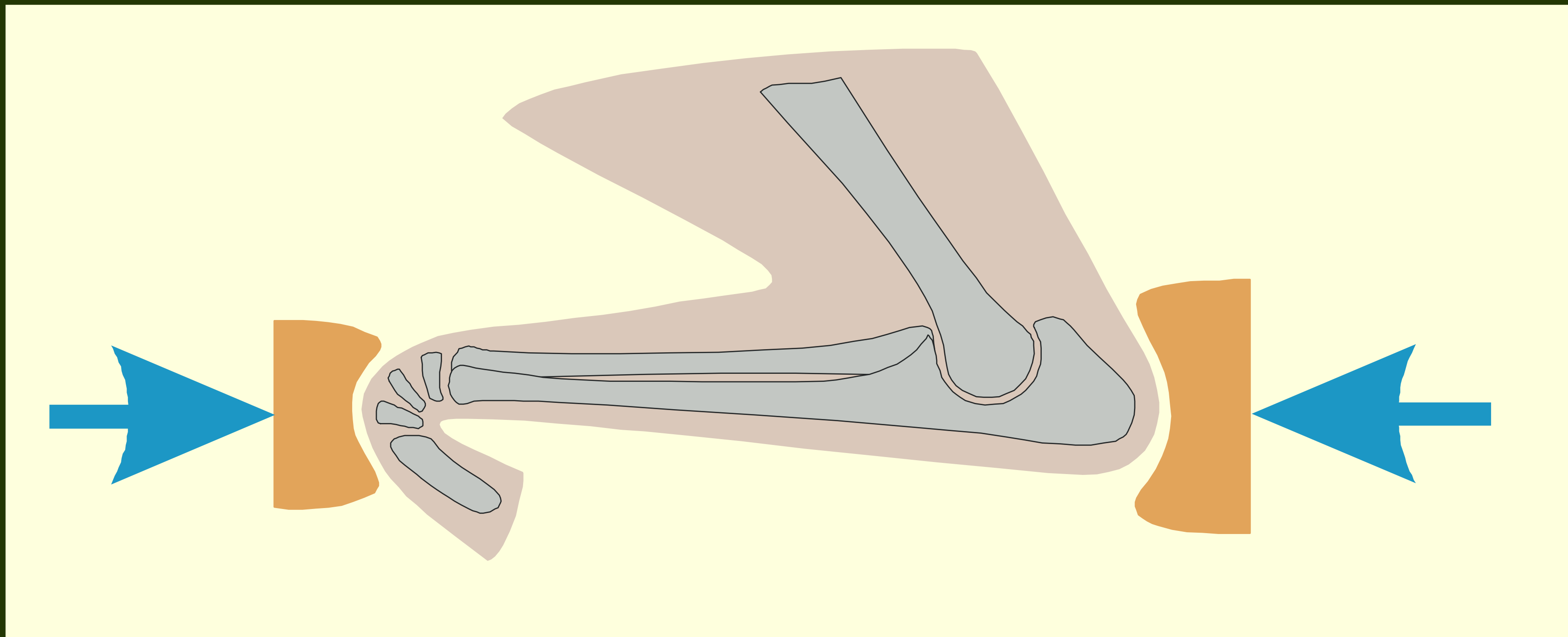
- Evidence of loading is retained by bone cells and this can modify subsequent responses to load

Consequences of mechanostat function

- Not all responses of bone cells to load are part of the adaptive response

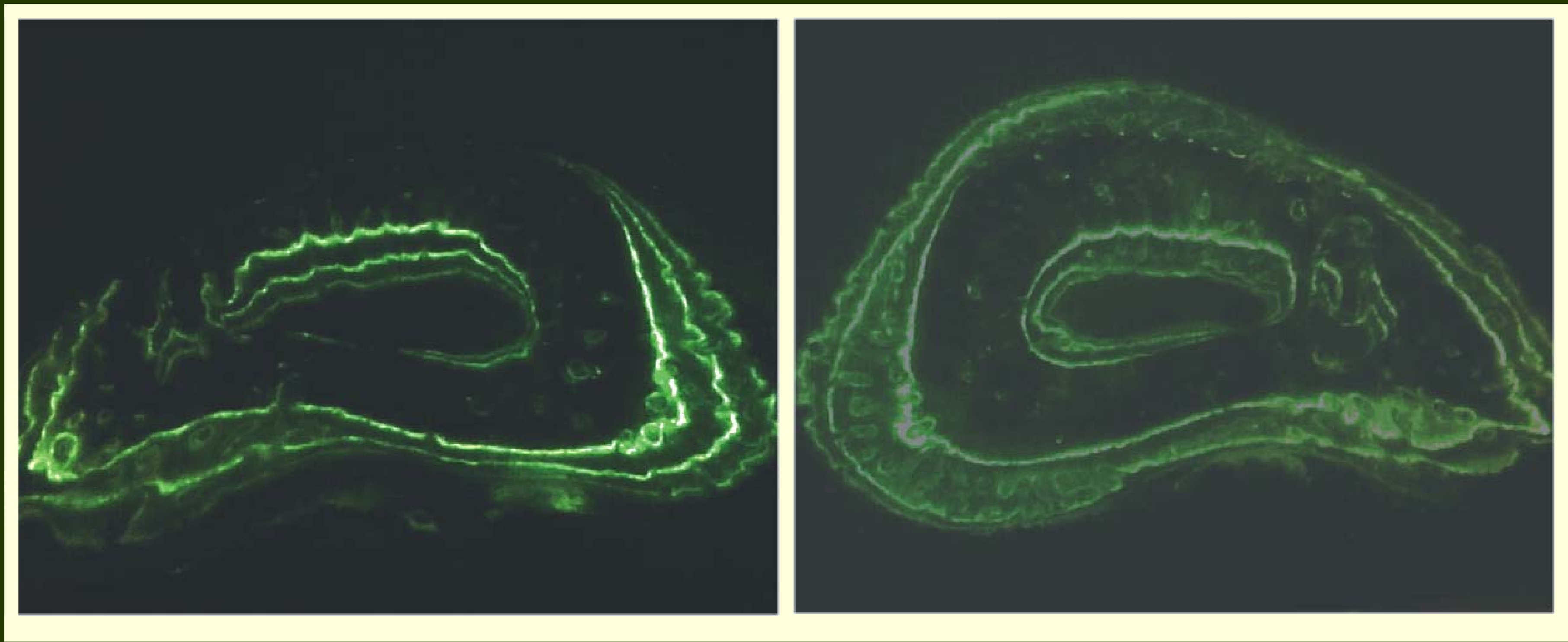
- Systems in the adaptive pathway fulfil known mechanostat properties


Age
Gender
Genotype
Diet
Environment
Intercellular communication
Effects of exercise

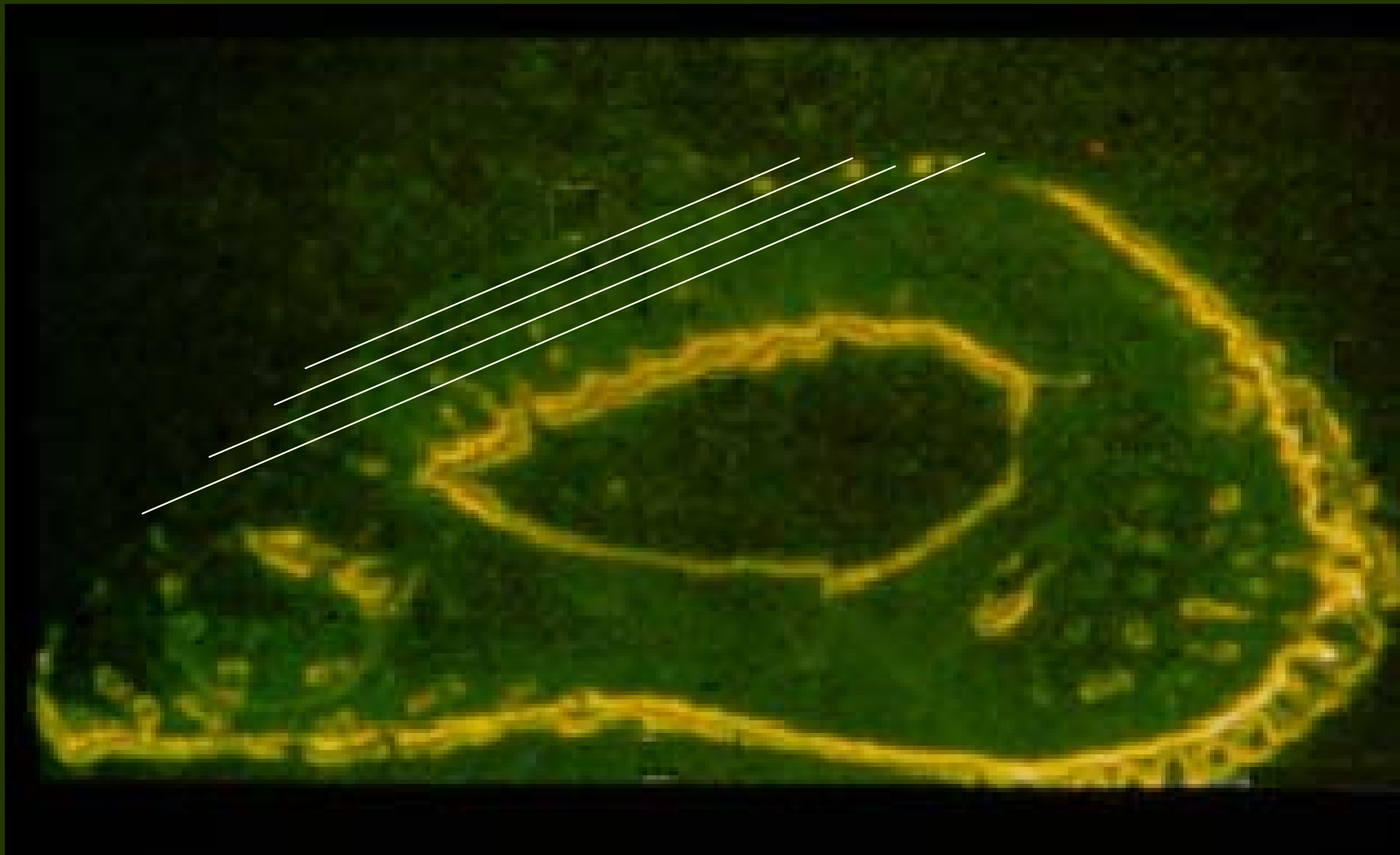


Torrance *et al* 1994

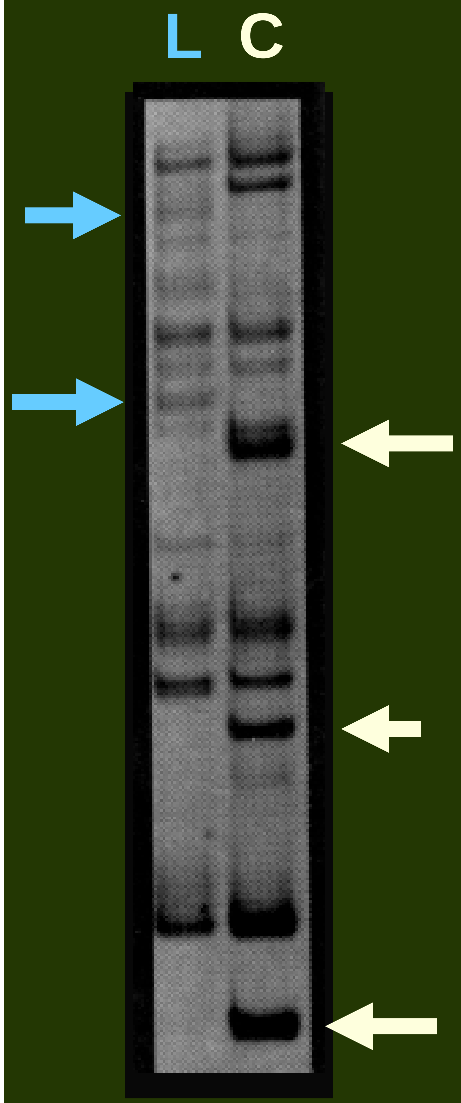
Load induced bone formation *in vivo*

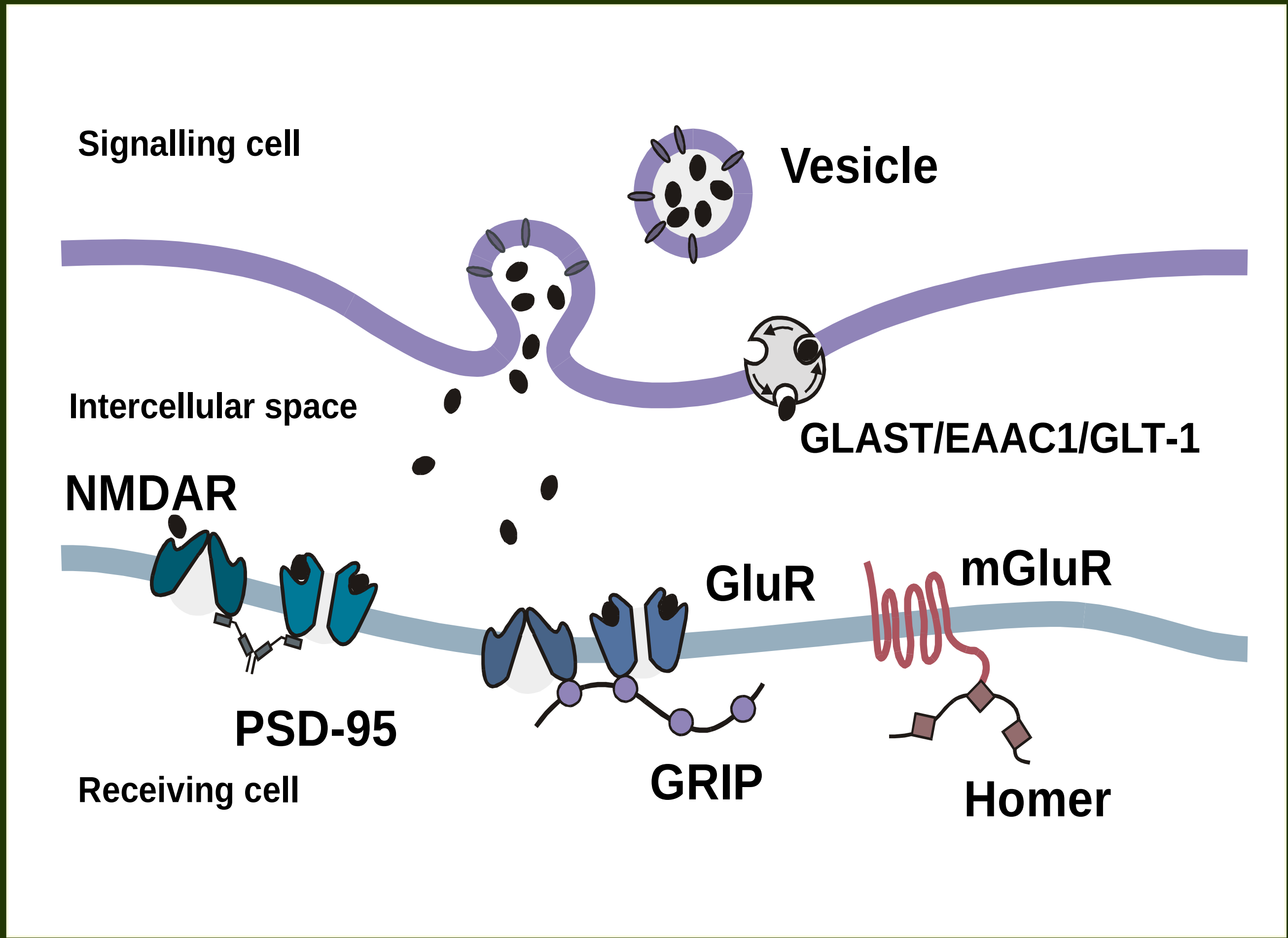


Control   Loaded

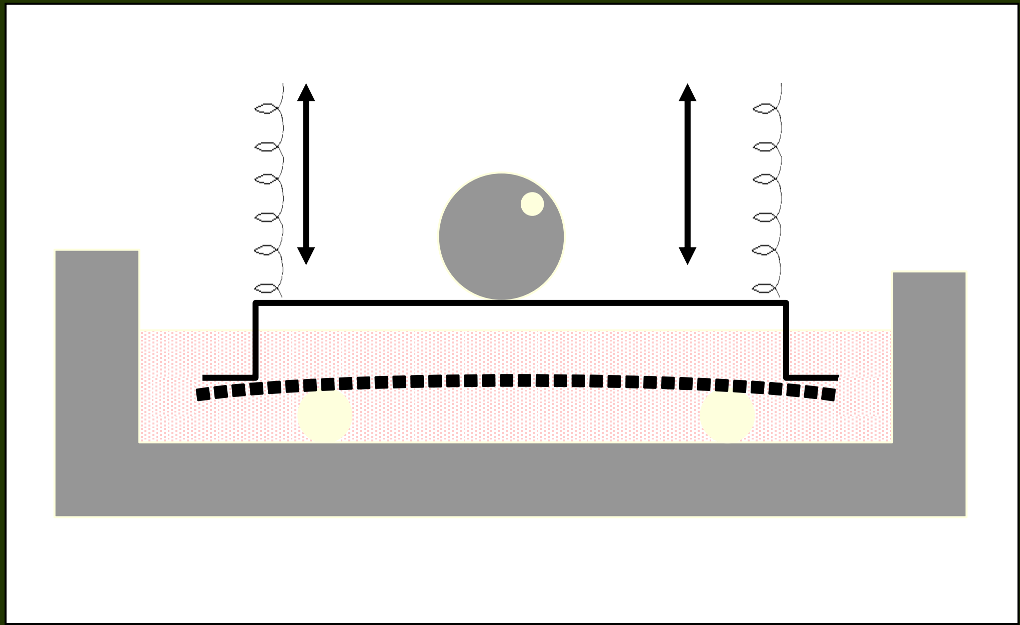


50 tangential cryostat sections (1μm, -35^{o}C), after removing periosteum



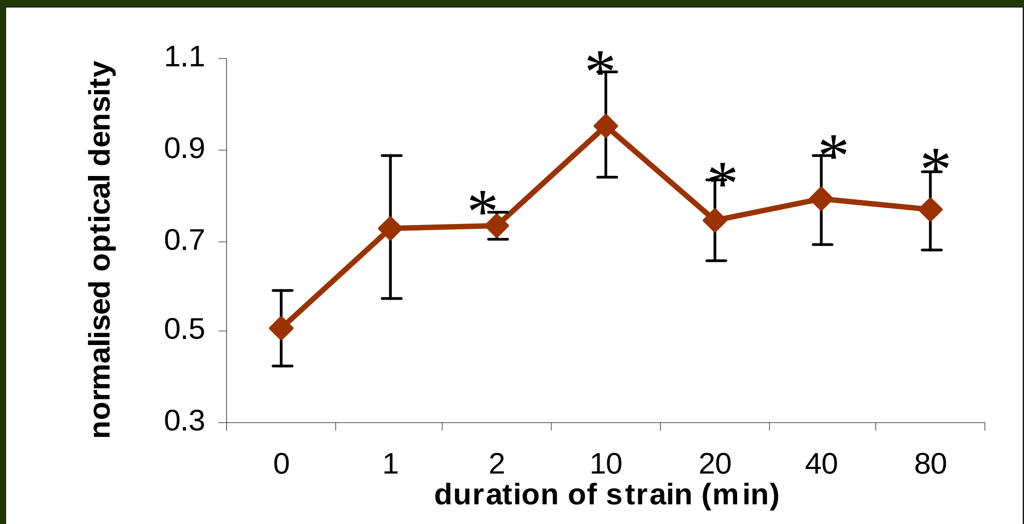


Mason *et al* Bone 1997



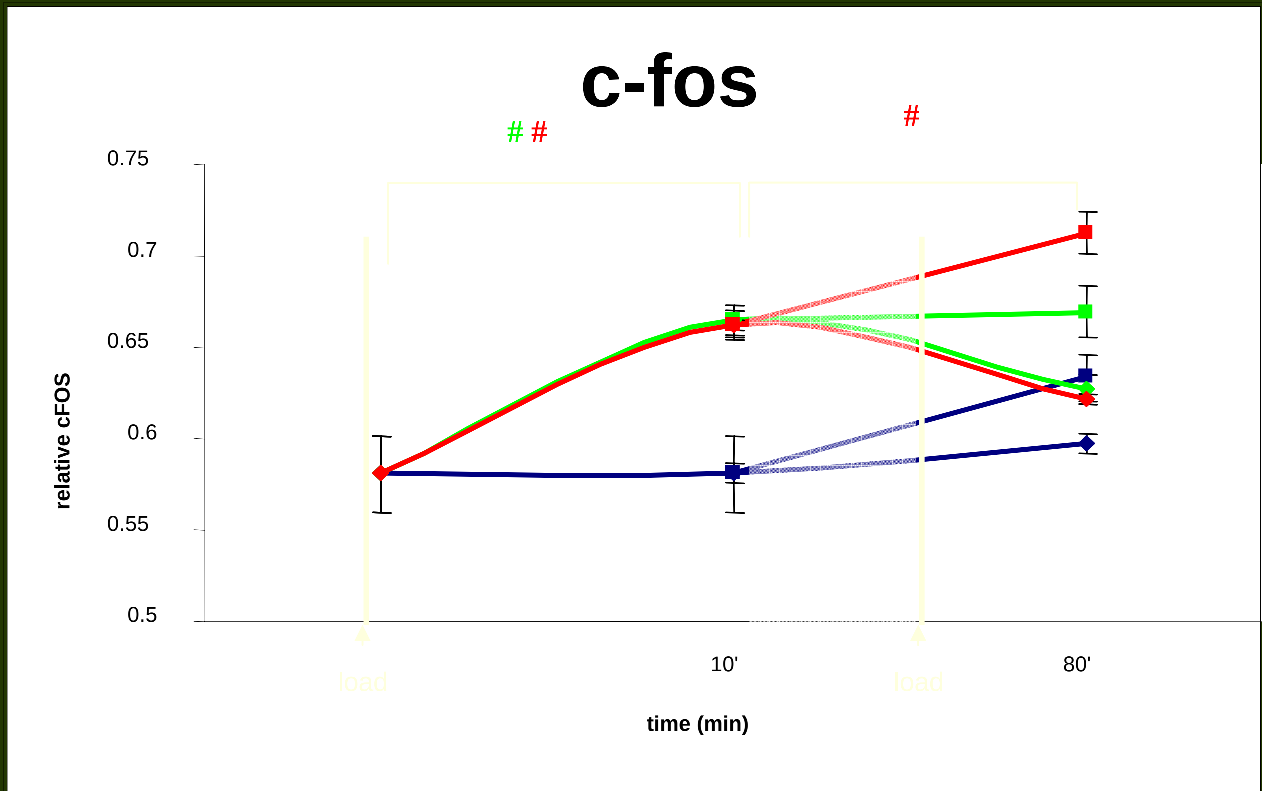
Loading in vitro

1 Hz
3400 microstrain
ROS17/2.8 cells



2 minutes/120 cycles
Saturates proliferative response to loading 48 hours later

One/two periods of loading, analysis at 10 and 80 minutes



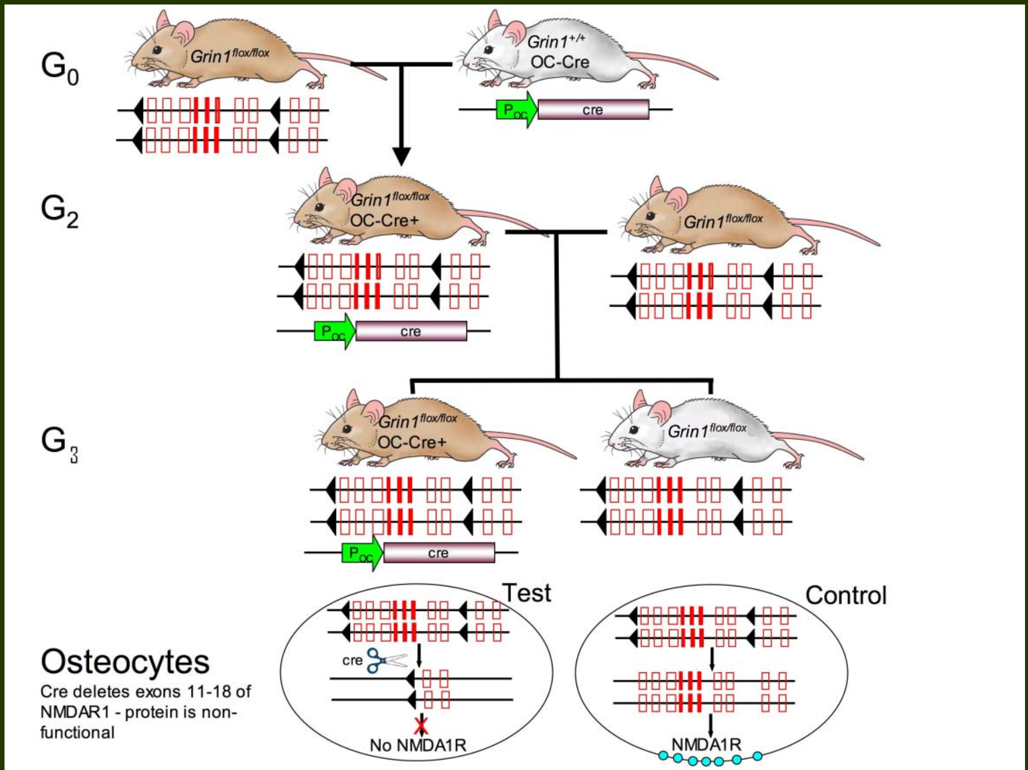
static control

shear

strain

Physiological role of glutamate in bone

- Glutamate receptors are essential for survival
- Knockout mice die at birth
- Tissue specific gene knockouts



Summary

- Bone is a composite material
- Makeup and properties vary according to function
- Resistance to fracture needs toughness
- Adaptive responses are complex
- The mechanostat regulates mass/architecture according to function

- Gareth Richards
- Dave Roberts
- Susana Martinez
- Brindha Ashok-Kumar
- Adi Desai
- Suruchi Pacharne

- Richard Hillam

- Amanda Patton
- Mark Birch
- Nicky Peet
- Paul Genever
- Gary Spencer
- Jamie Bhangu
- Deborah Mason
- Bev Fermor
- Alan Horner
- Liz Bowe
- John Burford
- Sarah Odoi
- Laura Parry

- Tom Clermens (UAB)
- Kathleen Caron (UNC)
- Rachel Davey (Melbourne)
- Larry Suva (Little Rock)
- Daniel Perren (Vanderbilt)

- ARC
- BBSRC
- Nuffield
- MRC
- Wellcome

- Medella Therapeutics

- Y0rkshire Forward