Orthodontic tooth movement

- Based on current understanding as we apply orthodontic force on tooth following changes in gross occurs

1. Primarily, alteration in the blood flow which results in reduced oxygen level at compressed area and might be an increased oxygen level at tension side.

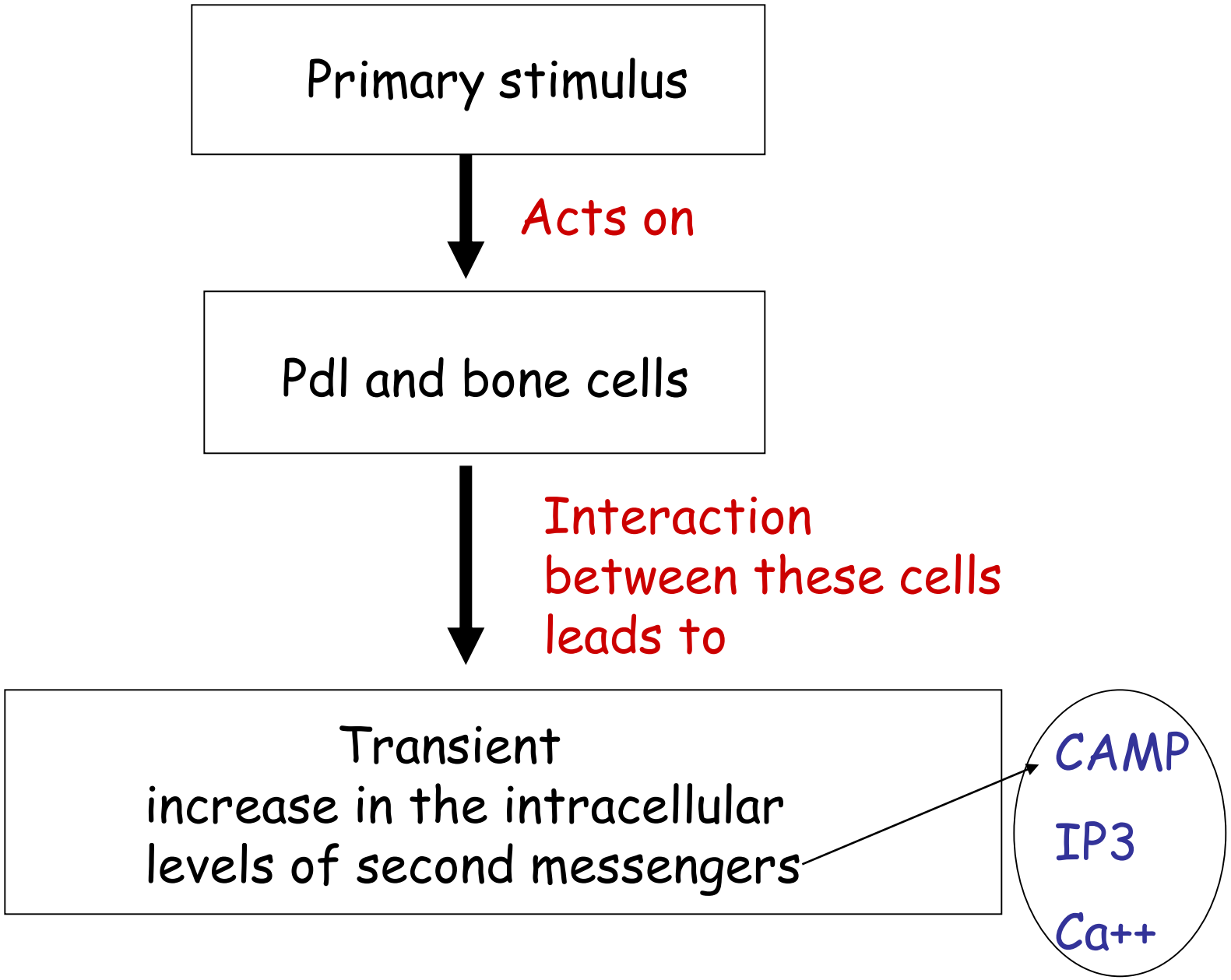
2. Secondly, generation of Piezo electric signal as now stated more appropriately as bioelectric potential in the form of small voltage of current which is released due to bending of bone and deformation of crystal structure.

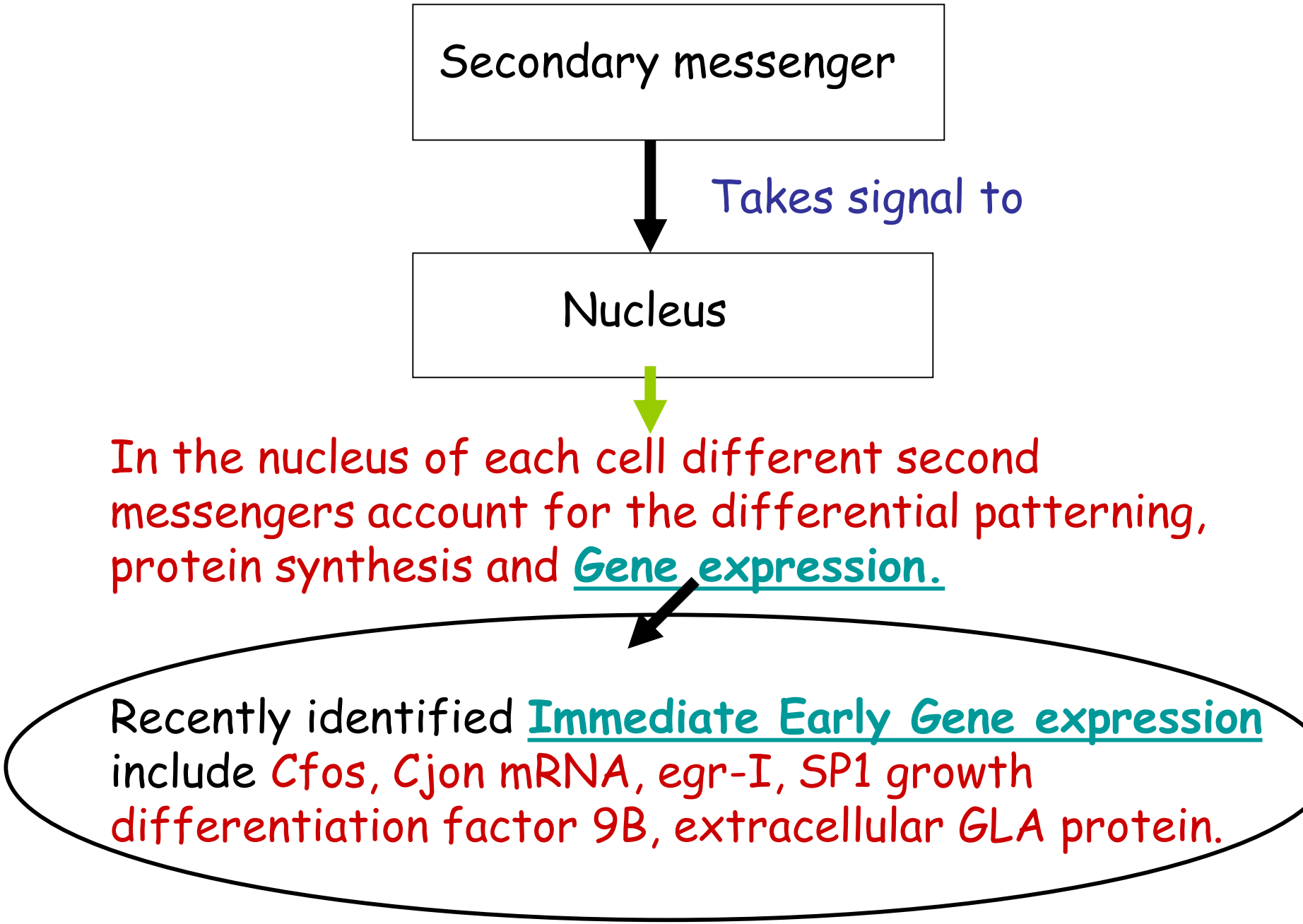
3. Thirdly, possibility of release of neuro transmitters (example Substance P, Vaso intestinal polypeptide VIP) on account of physical distortion imposed by peripheral forces on paradental tissues such as nerve fibers and terminals

Thus the primary stimulus such as that of orthodontic force may elicit its response to cell of PDL and bone in the form of release of

- Bioelectric signals produced on account of bone bending
- Chemical mediators such as prostaglandins, cytokines, Nitric oxide (NO) etc.,
- Release of neurotransmitters.

- It has been proved that cells in PDL and bone cells posses receptors for these substances (i.e. primary stimulus) and all these are highly interacting and interconnected.


Primary stimulus
Acts on
Pdl and bone cells
Interaction
between these cells
leads to
Transient
increase in the intracellular
levels of second messengers
CAMP
IP3
Ca++


Secondary messenger
Takes signal to
Nucleus
In the nucleus of each cell different second messengers account for the differential patterning, protein synthesis and Gene expression.
Recently identified Immediate Early Gene expression include Cfos, Cjon mRNA, egr-I, SP1 growth differentiation factor 9B, extracellular GLA protein.

- These transcription factors can produce either cellular proliferation or cellular differentiation leading to osteoblastic bone formation or osteoclastic bone resorption.

ROLE OF PROSTAGLANDINS IN MEDIATING OTM

- Arachidonic acid can be released either by phospholipidases activated by direct cellular damage or by any nondestructive perturbation of the membrane, be it *physical, chemical, hormonal or neuro hormonal.*
- Prostaglandins can also be termed as local hormones functioning to co-ordinate effects of those other hormones which induce prostaglandin synthesis and Prostaglandins function through G-protein linked receptors to elicit their cellular effects.

- Classically Prostaglandins as one of the mediators of inflammation cause an increase in intracellular CAMP and Calcium accumulation by Monocytic cells which then modulates and activates osteoclastic activity.
- Klein and Riasz in 1970 reported first time the involvement of Prostaglandins in OTM.

- Recent studies indicate that Prostoglandins increase the number of Osteoclasts as well as stimulate Osteoblastic cell differentiation and new bone formation.

CYTOKINES & GROWTH FACTORS IN OTM

- Cytokines secreted by leukocytes may interact directly with bone cells or indirectly, via neighboring cells, such as monocytes/macrophages,lymphocytes and fibroblasts, through their production of cytokine, or a variety of Growth factors.
- Cytokines released have multiple activities, which include bone remodeling, bone resorption, new bone deposition.

Prominent cytokines

- Interleukin I,
- IL-6,
- Tumor necrosis factor,
- Granulocyte- macrophage colony stimulating factor (GM-CSF)
- Macrophage colony stimulating factor (M-CSF).

- Growth Factors are also released during inflammation and repair by the cells of PDL and bone.

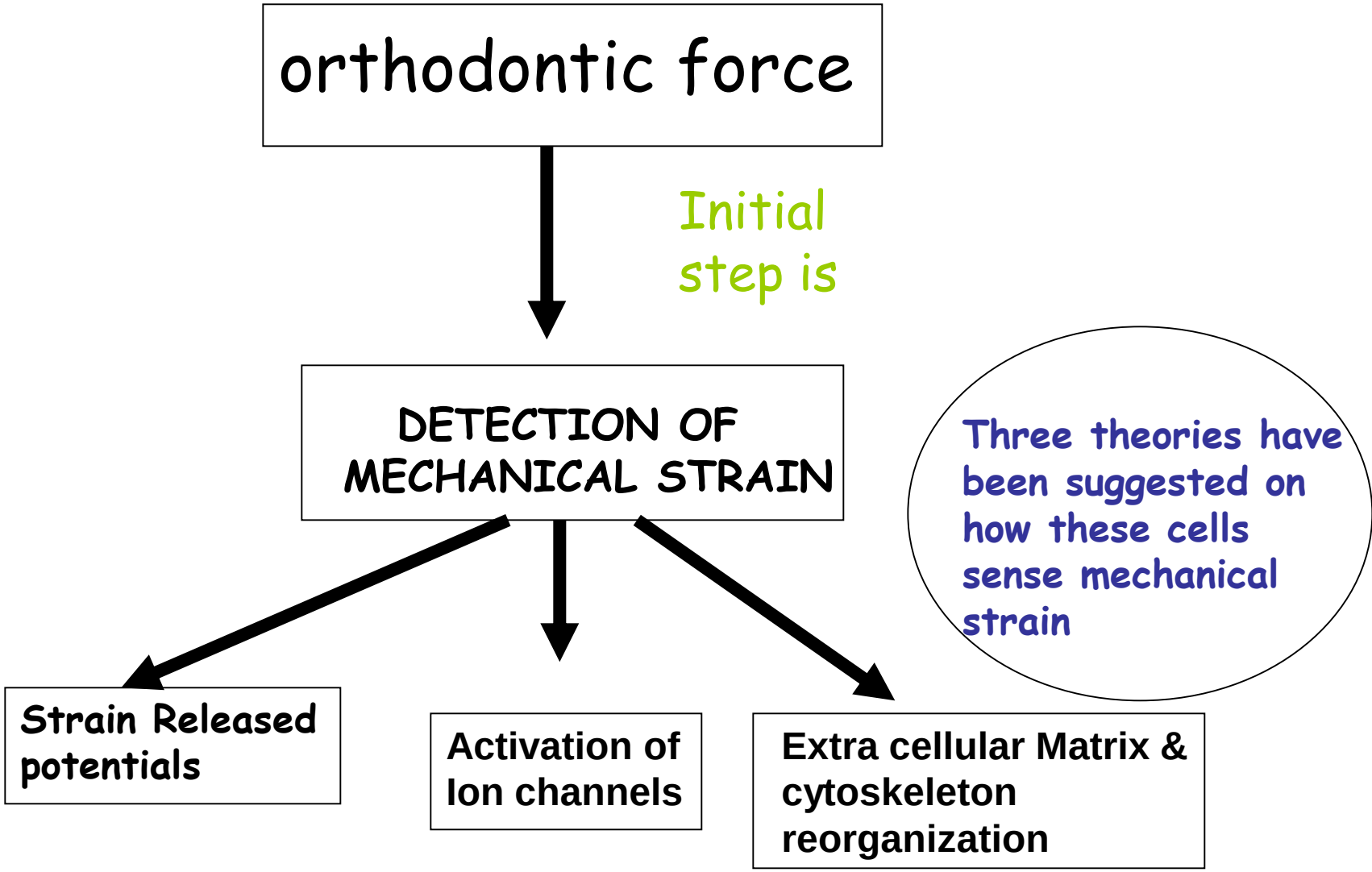
- Another theory stated that the growth factors may secreted by bone cells and stored (bound to bound matrix)

Growth Factors

- Fibroblast Growth Factor (b FGF & a FGF),
- Insulin like Growth Factors (IGF – I, IGF – II),
- Transforming Growth Factor (TGF),
- Platelet Growth Factor (PDGFS),
- Bone Morphogenic Proteins (BMP)

- VEGF (recombitent human vascular endothelial Growth Factor) has shown to stimulate macrophage colony stimulating factor, thereby enhancing number of osteoclasts and thus increased rate of OTM.

DETECTION OF MECHANICAL STRAIN BY BONE CELLS

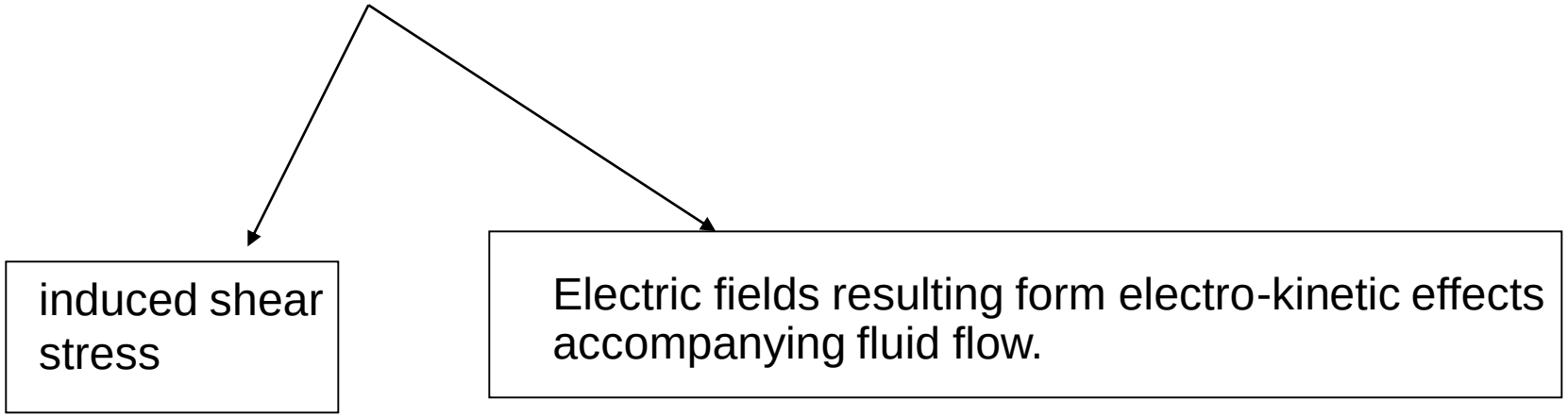


A) STRAIN RELEASED POTENTIALS

- Application of small bending forces to bones is known to produce flow of interstitial fluid, through the canalicular network, generating streaming potentials.
- Osteocytes are more sensitive to mechanical stress than osteoblasts which are more sensitive than fibroblasts.

Application of forces to bone results in several potential stimuli to bone cell function,

- Hydrostatic pressure
- Direct cell strain,
- Fluid flow



Events affecting osteocytes → **Activates osteoblasts** or **Activates osteoclasts**

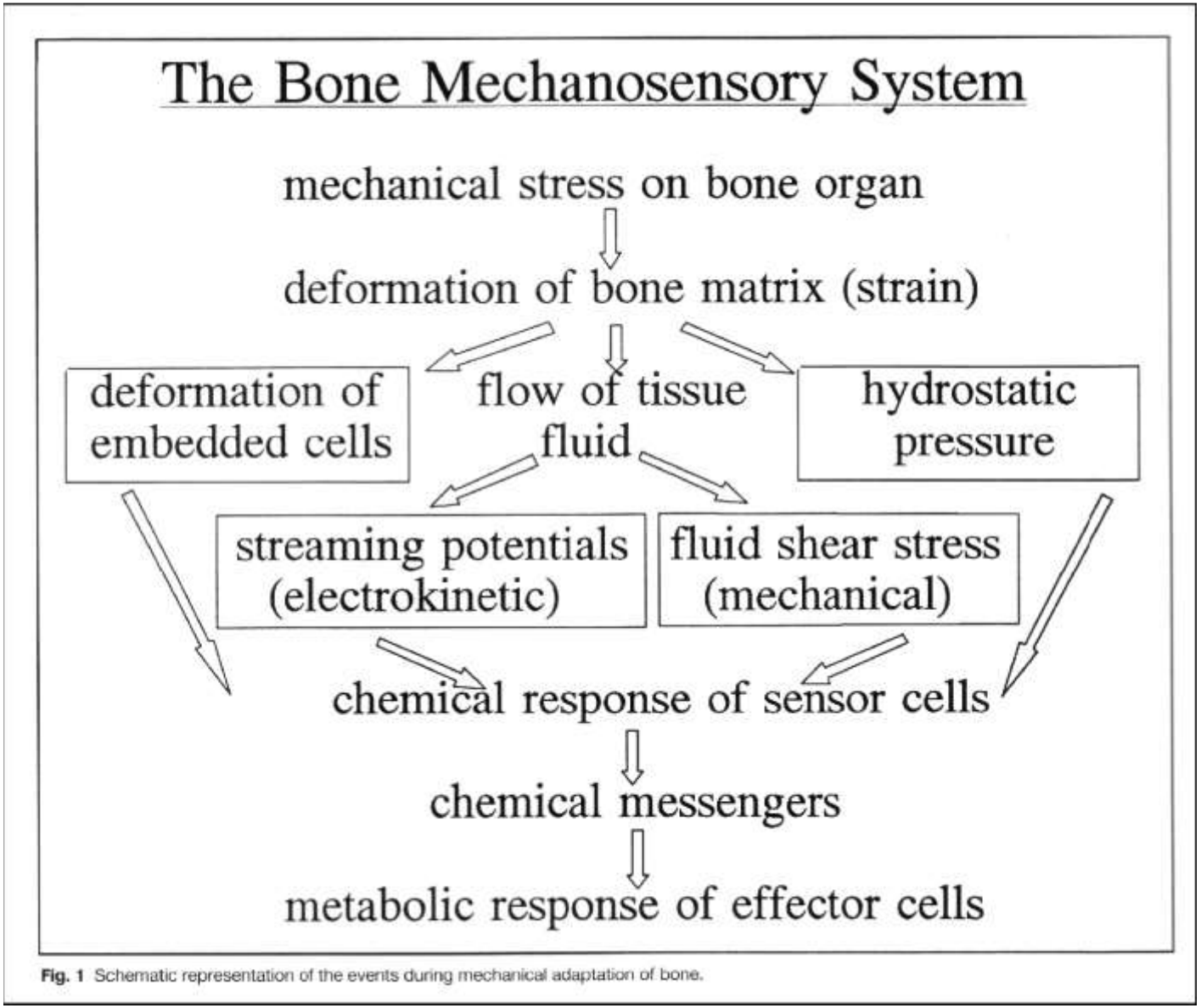


Fig. 1 Schematic representation of the events during mechanical adaptation of bone.

B) ACTIVATION OF ION CHANNELS

- *Ion Channels are tunnel shaped proteins that cross the width of cell membrane and serve as selective conductive pathways for ions that cross the membrane as well as membranes surrounding intracellular organelles.*

Ion channels can be divided in to groups depending upon type of stimulus needed to activate the channel.

Major groups are

- Voltage gated → **Response to changes in transmembrane potential.**
- Ligand gated → **specific ligands that may attach to the cell membrane near channel opening.**
- Mechanosensitive (stretch) ion channels.

↓

react to structural perturbations.

EXTRACELLULAR MATRIX & CYTOSKELETON REORGANIZATION.

- The macromolecules which make up the ECM include collagen & glycose amino glycans.
- These macromolecules are secreted at local levels by cells, particularly fibroblast in the PDL & osteoblast in the bone. The matrix metallo proteins (MMPS) represents major class of enzymes responsible for ECM metabolism.