REGENERATIVE BIOLOGY AND MEDICINE: RESEARCH OPPORTUNITIES FOR PHYSICISTS, ENGINEERS, MATHEMATICIANS

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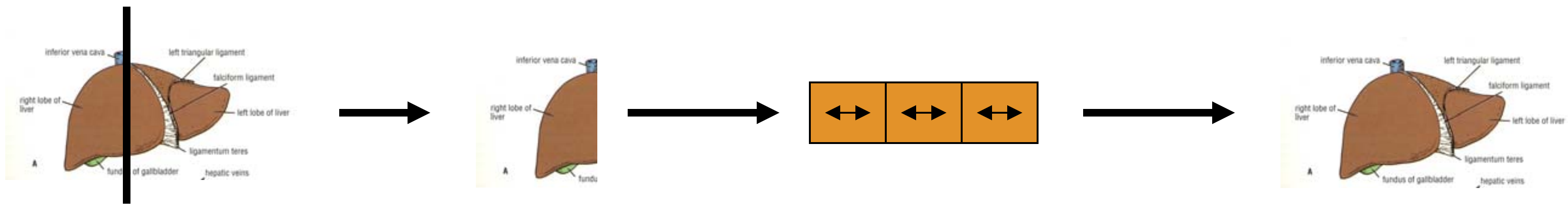
DEFINITIONS

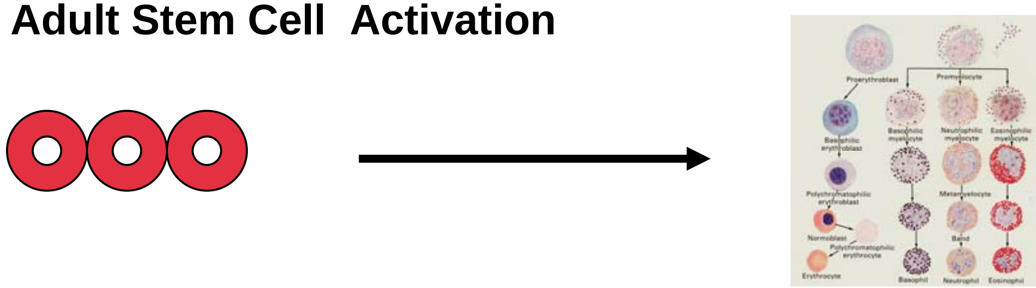
- REGENERATIVE BIOLOGY: STUDY OF THE MECHANISMS OF REGENERATION AT MOLECULAR, CELLULAR, TISSUE, ORGAN AND APPENDAGE LEVELS
- REGENERATIVE MEDICINE: TRANSLATION OF RESEARCH ON REGENERATIVE MECHANISMS INTO THERAPIES THAT PROMOTE THE REGENERATION OF REGENERATION-DEFICIENT STRUCTURES

MECHANISMS OF REGENERATION AT THE ORGAN AND TISSUE LEVEL

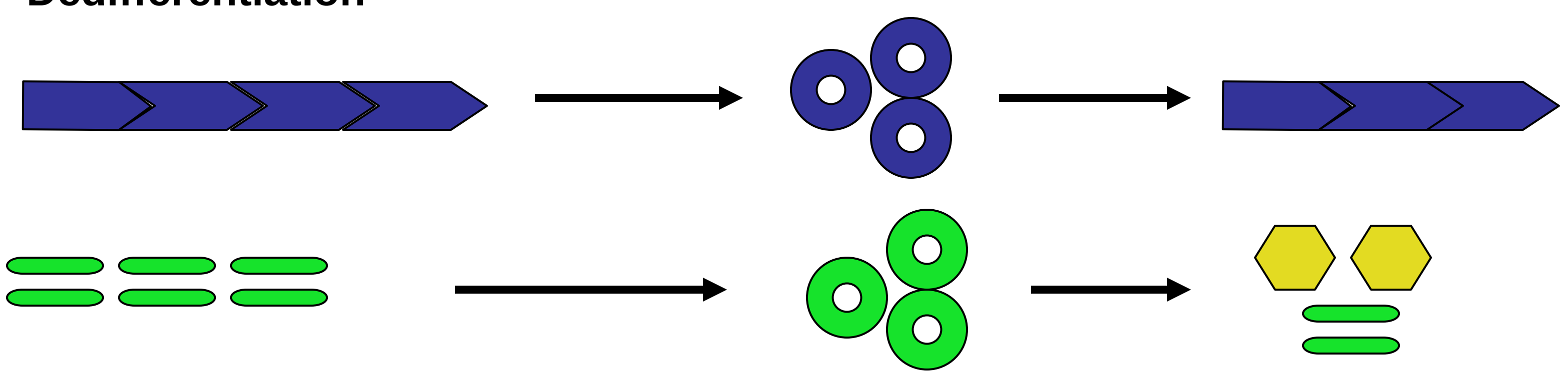
Compensatory Hyperplasia



Adult Stem Cell Activation

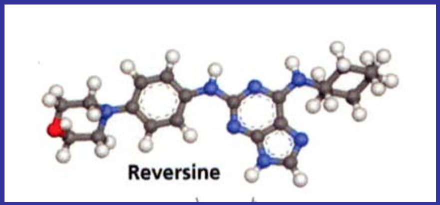


Dedifferentiation

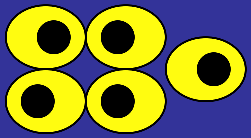


STRATEGIES OF REGENERATIVE MEDICINE

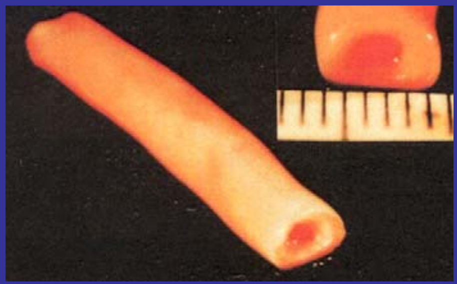
CHEMICAL INDUCTION

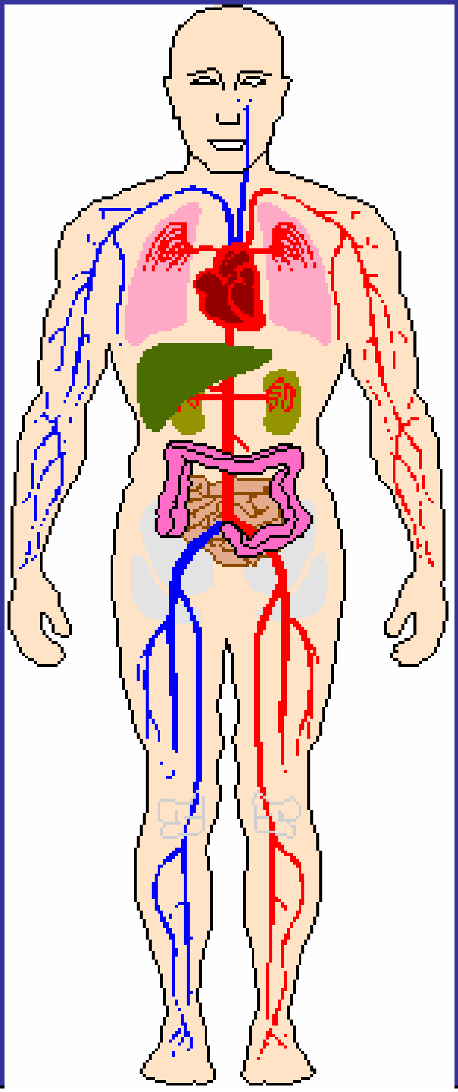


CELL TRANSPLANTS

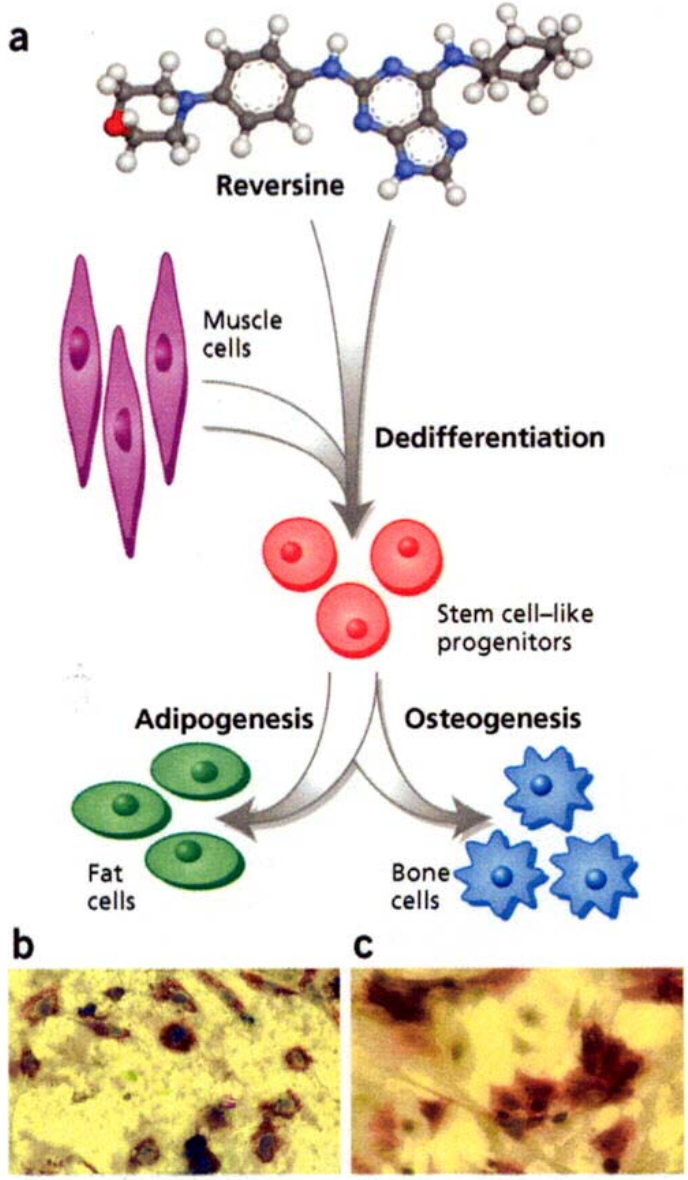


BIOARTIFICIAL TISSUE

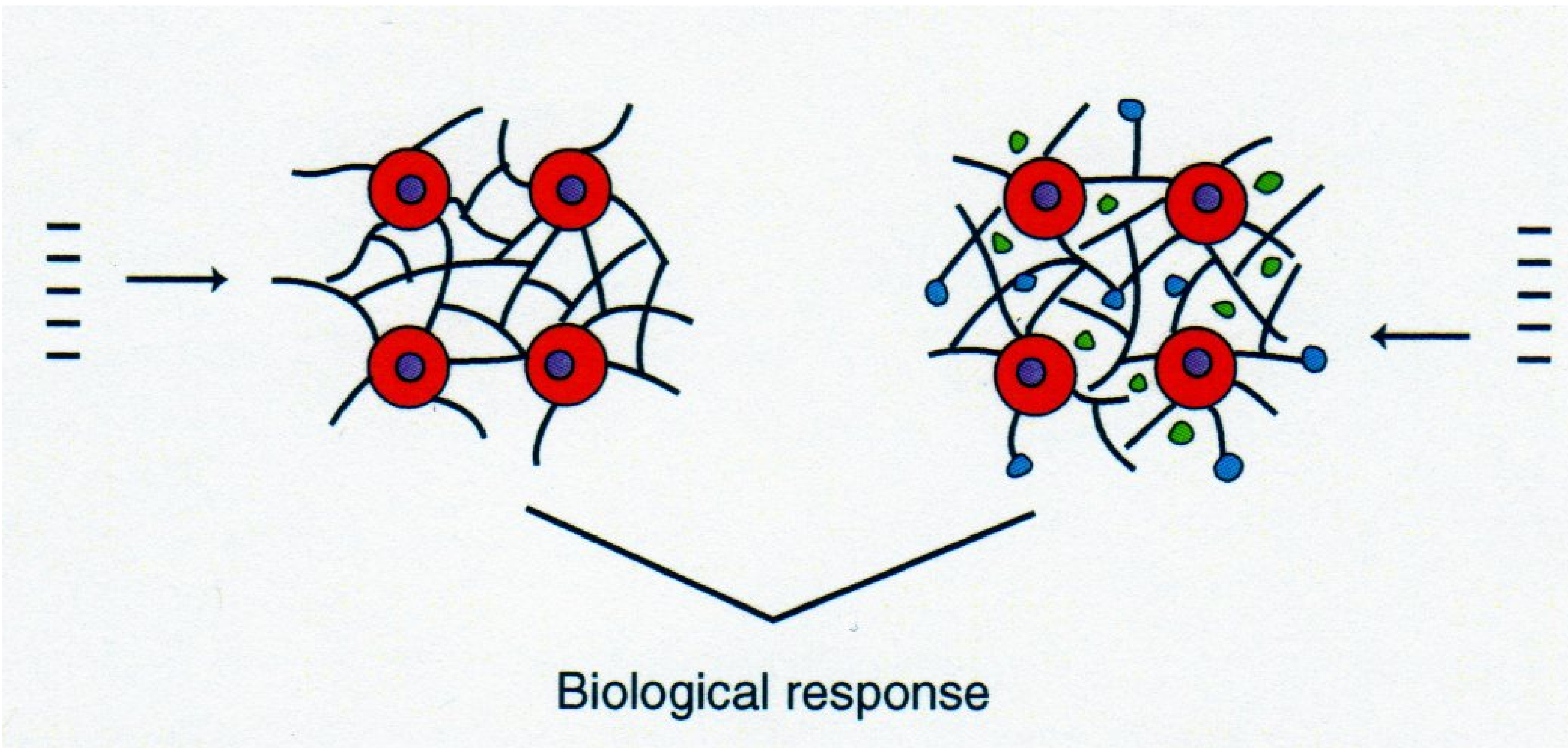




CHEMICAL INDUCTION OF REGENERATION

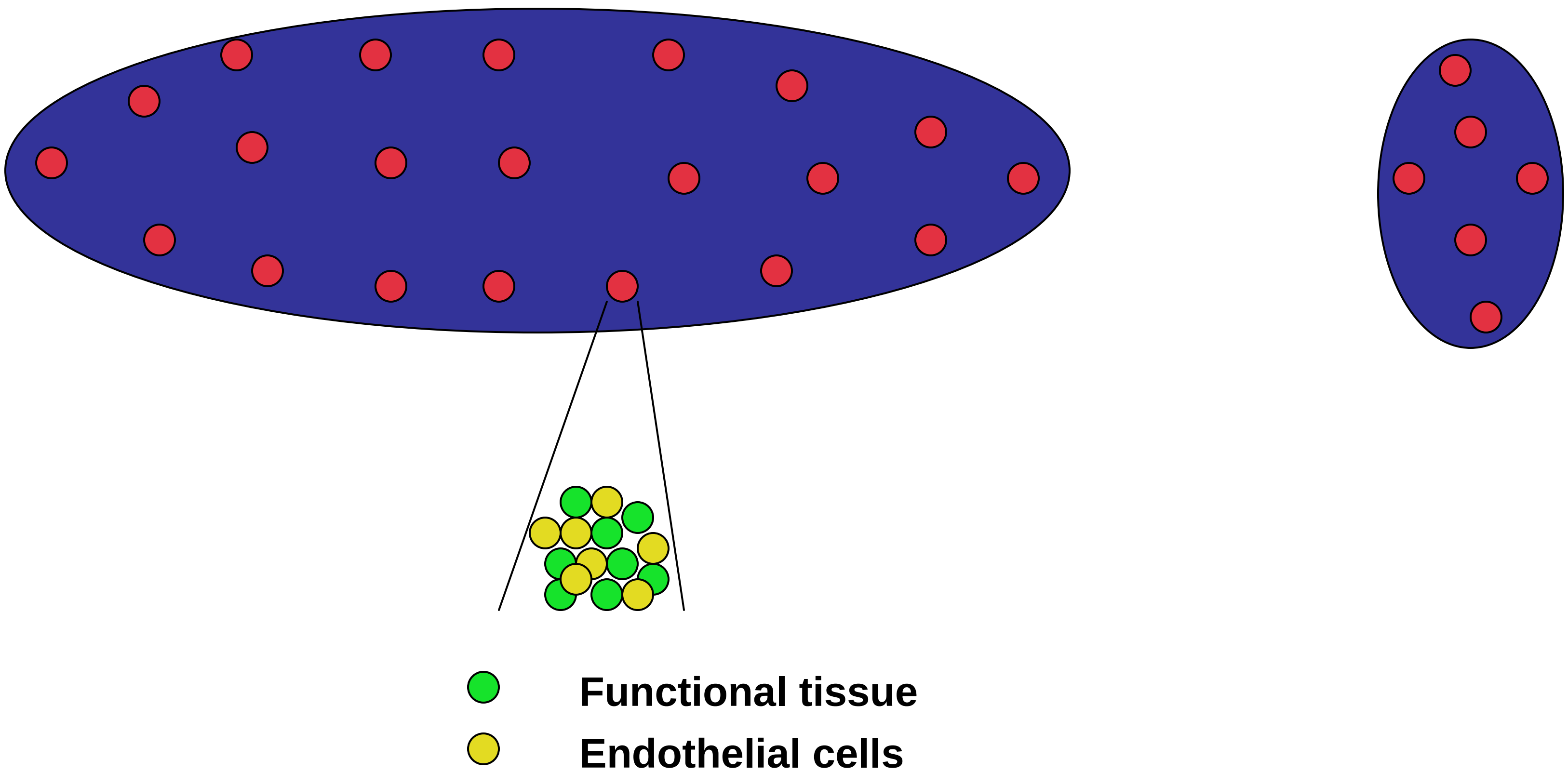


CHEMICAL INDUCTION OF REGENERATION



SCREENING ECM MOLECULES FOR EFFECTS ON CELLS AND SCREENING LIBRARIES OF SOLUBLE MOLECULES FOR THEIR EFFECTS ON CELLS TETHERED TO ECM MOLECULES

BUILDING A BIOARTIFICIAL TISSUE



PHYSICS/CHEMISTRY/ENGINEERING PROBLEMS

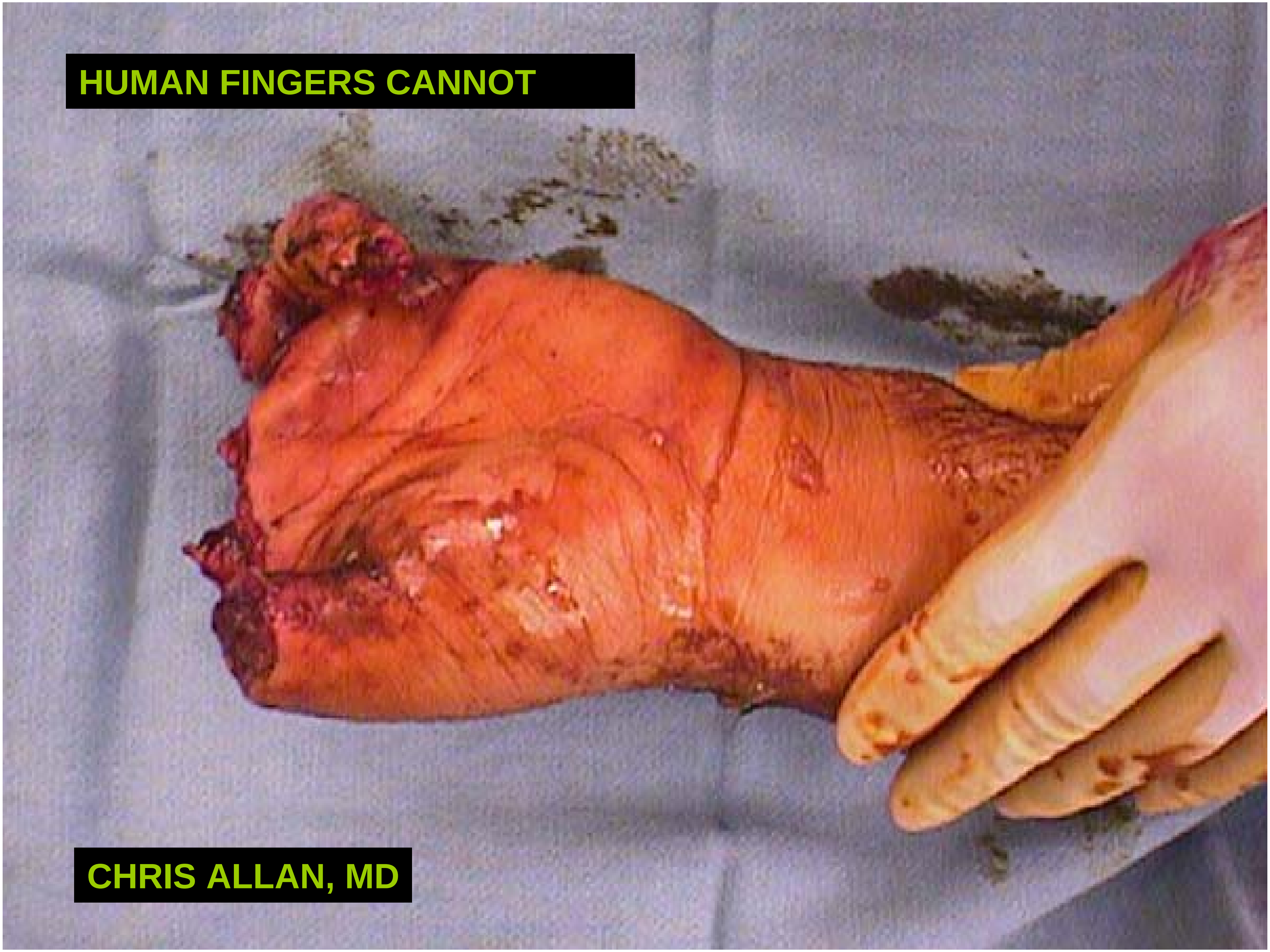
- **DELIVERY SYSTEMS (MOLECULES, CELLS)**
- **STRENGTH OF REPAIRED TISSUES**
- **CELL PRESERVATION**
- **PHYSICS/CHEMISTRY OF BIOMATERIALS (POROSITY, PIEZOELECTRIC EFFECTS, MOLECULAR ORIENTATION, ADHESIVENESS, ABILITY TO INCORPORATE BIOFACTORS, KINETICS OF BIOFACTOR RELEASE, INTEGRATION WITH HOST TISSUE**

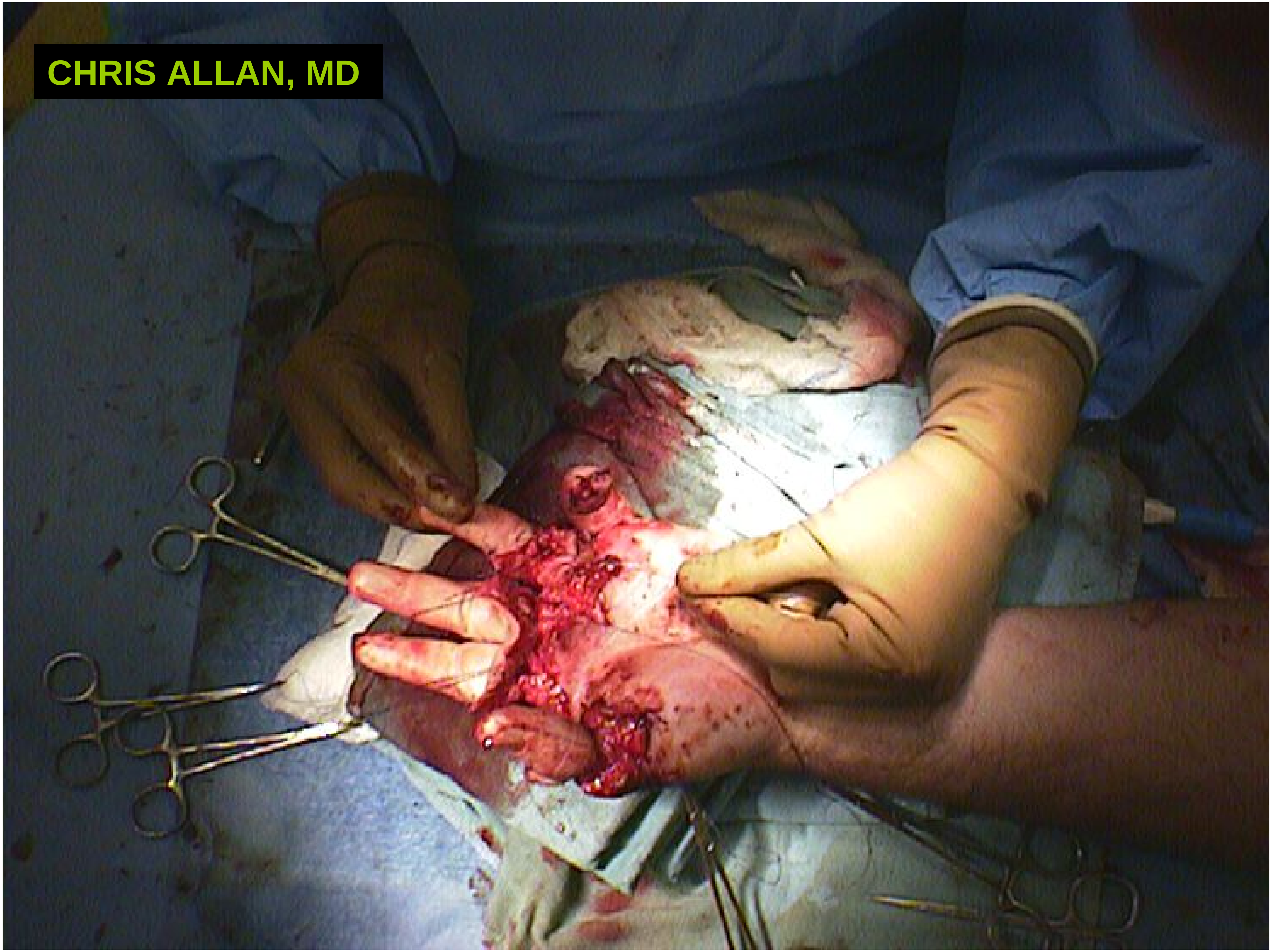
APPENDAGES

A

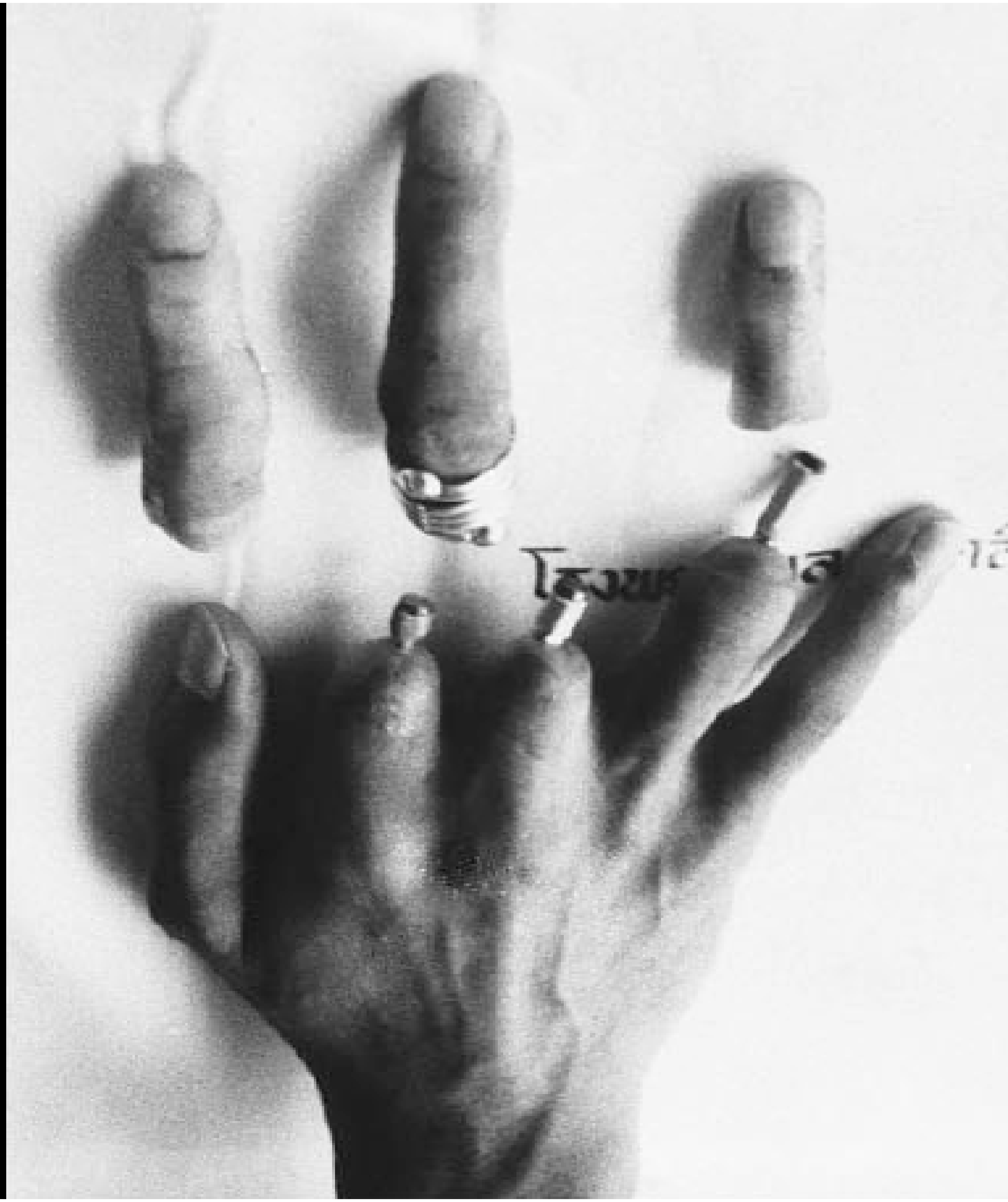
B

HUMAN FINGERTIPS CAN REGENERATE

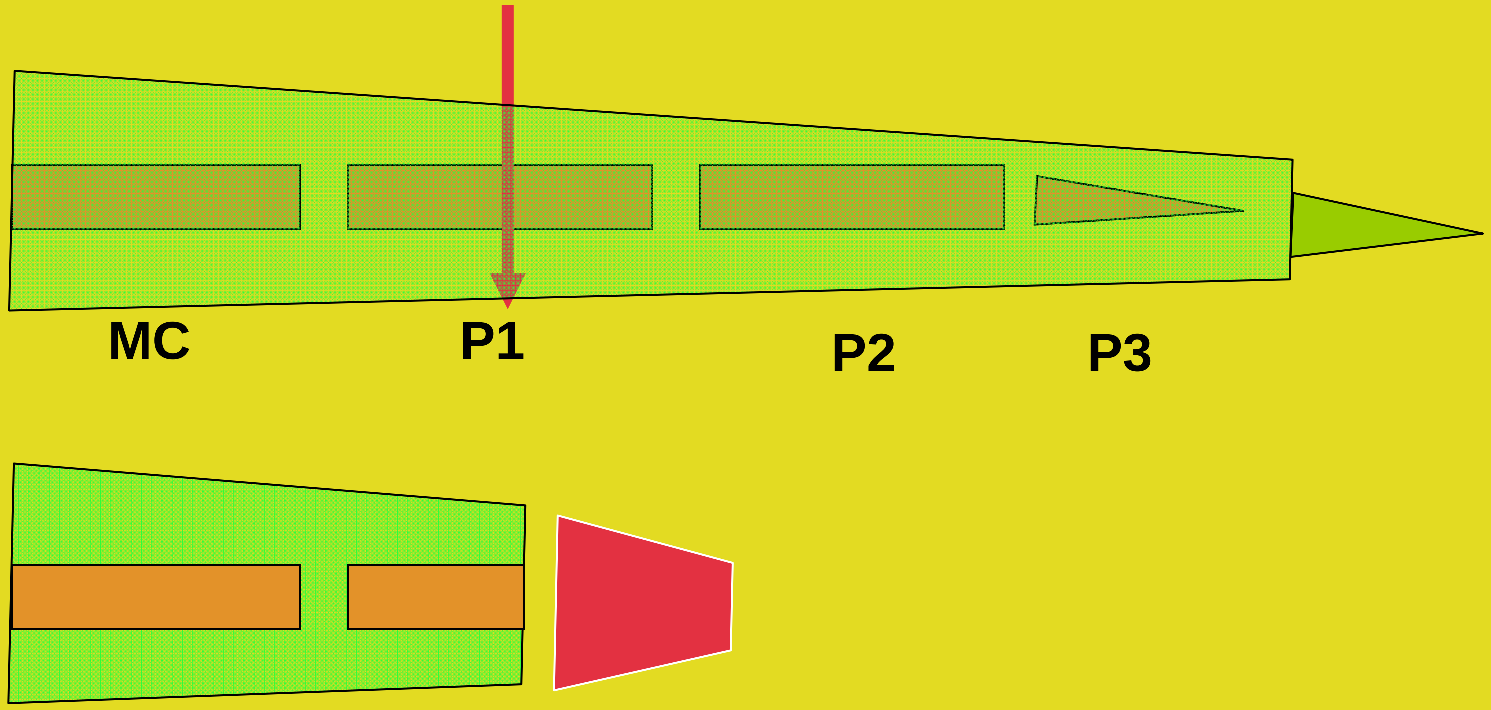

HUMAN FINGERS CANNOT
CHRIS ALLAN, MD


CHRIS ALLAN, MD


CHRIS ALLAN, MD



COULD WE USE A TEMPLATE LOADED WITH REGENERATION-PROMOTING MOLECULES TO REGENERATE A FINGER?



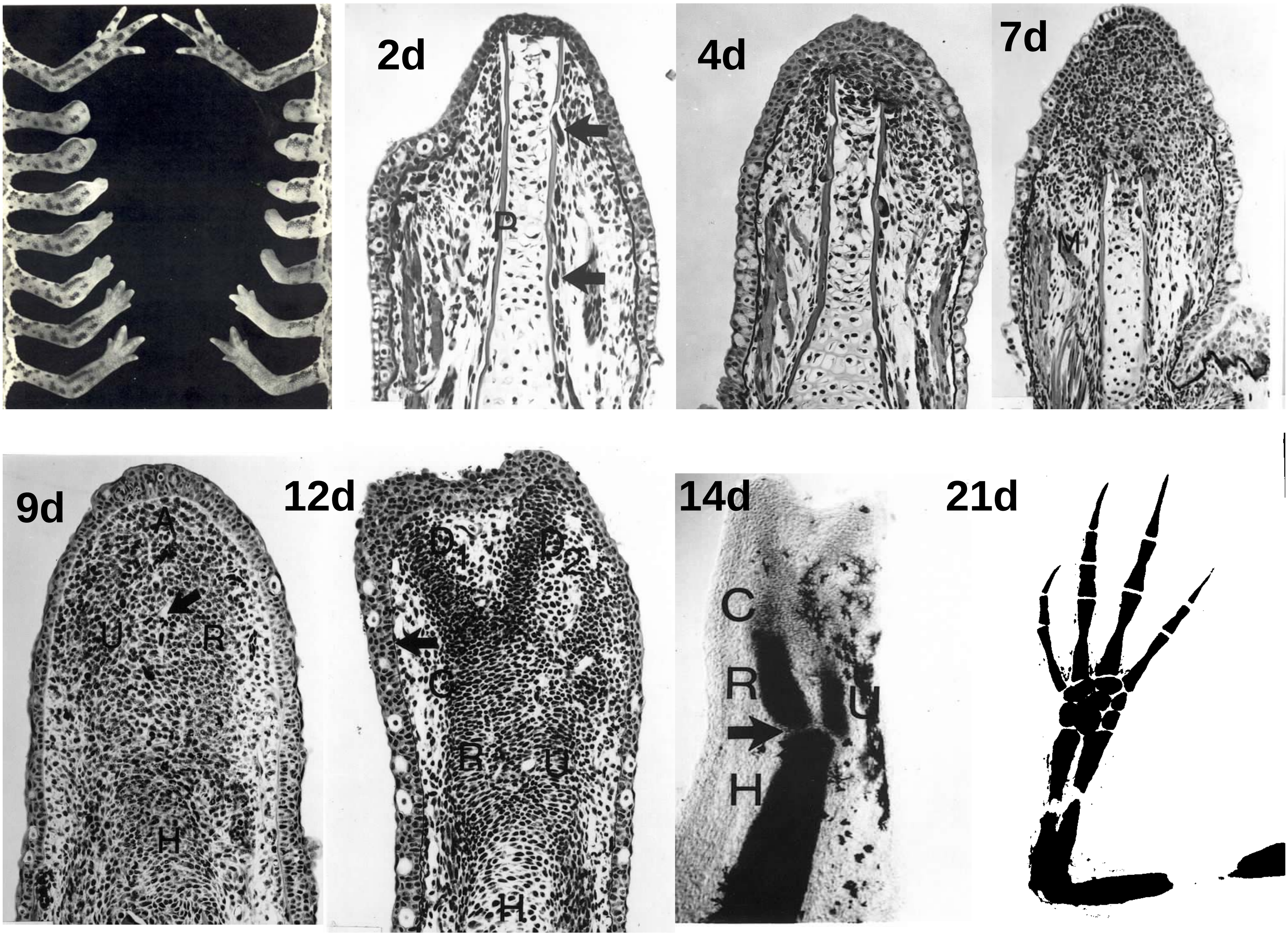
POTENTIAL MOLECULES TO TEST

- SIGNALING MOLECULES INVOLVED IN REGENERATION
- SUPPRESSANTS OF MOLECULES INVOLVED IN SCARRING
- SMALL MOLECULES

  --RETINOIC ACID

  --REVERSINE
- MOLECULES IDENTFIED BY GENOMICS AND/OR PROTEOMICS
- COMBINATIONS

REGENERATION OF WHOLE LIMBS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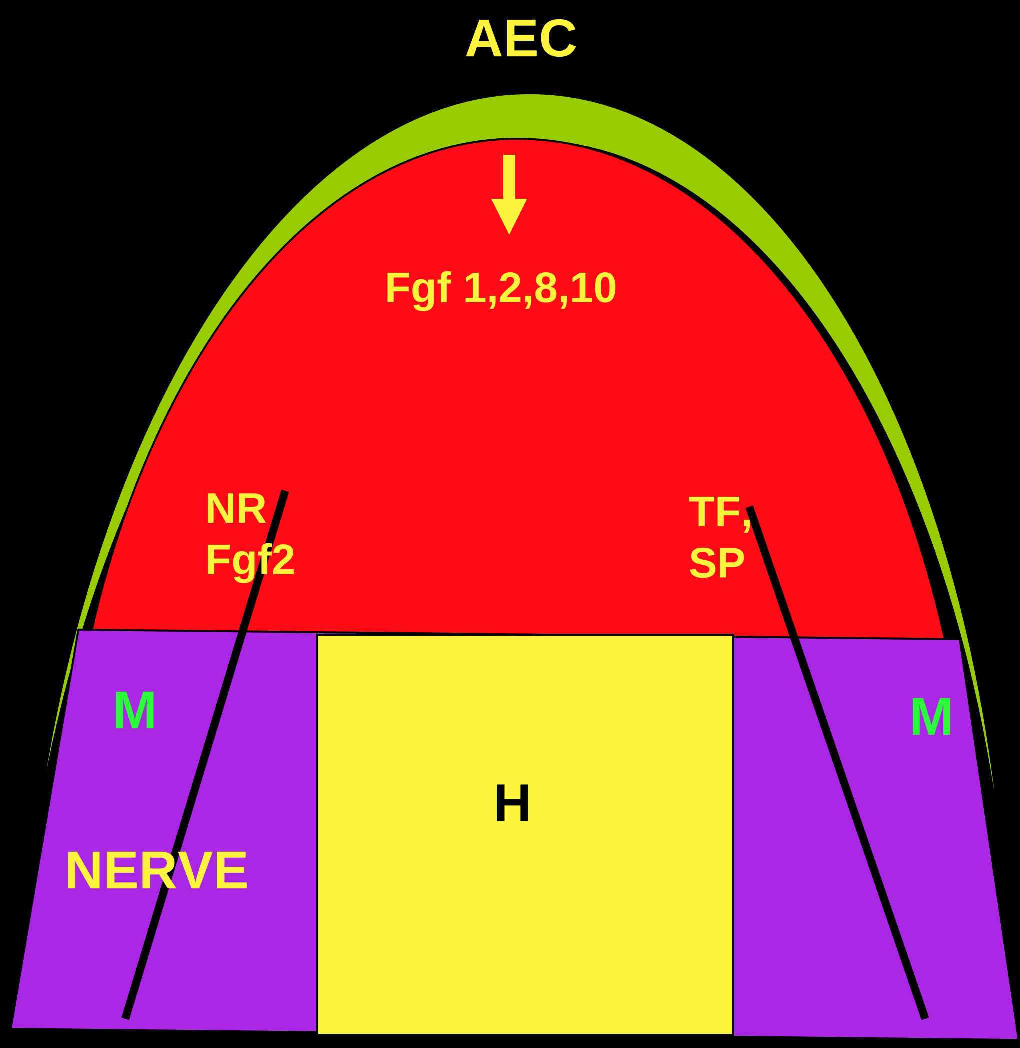
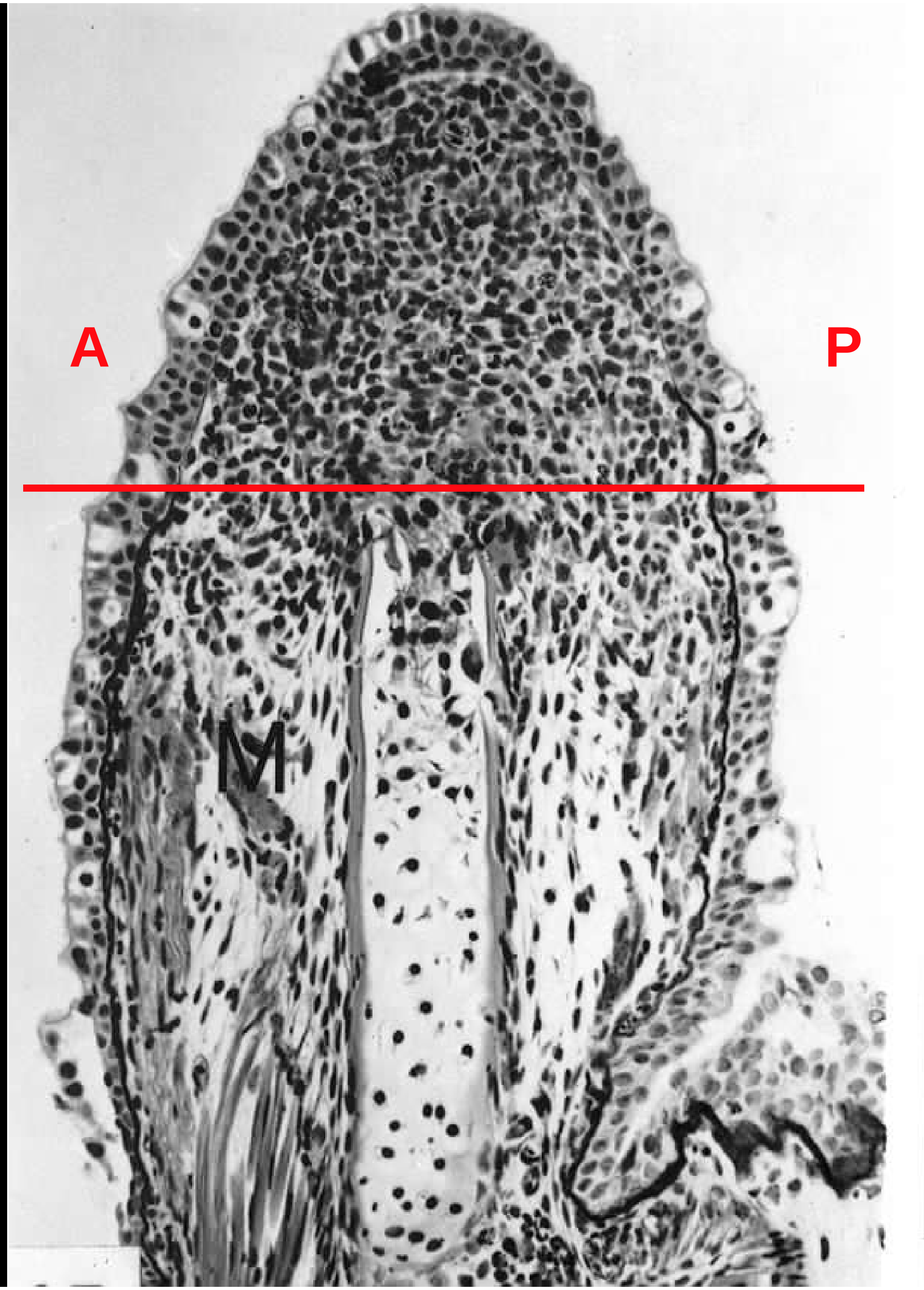
BLASTEMA CELL SURVIVAL AND PROLIFERATION FACTORS



THE BLASTEMA IS A SELF-ORGANIZING SYSTEM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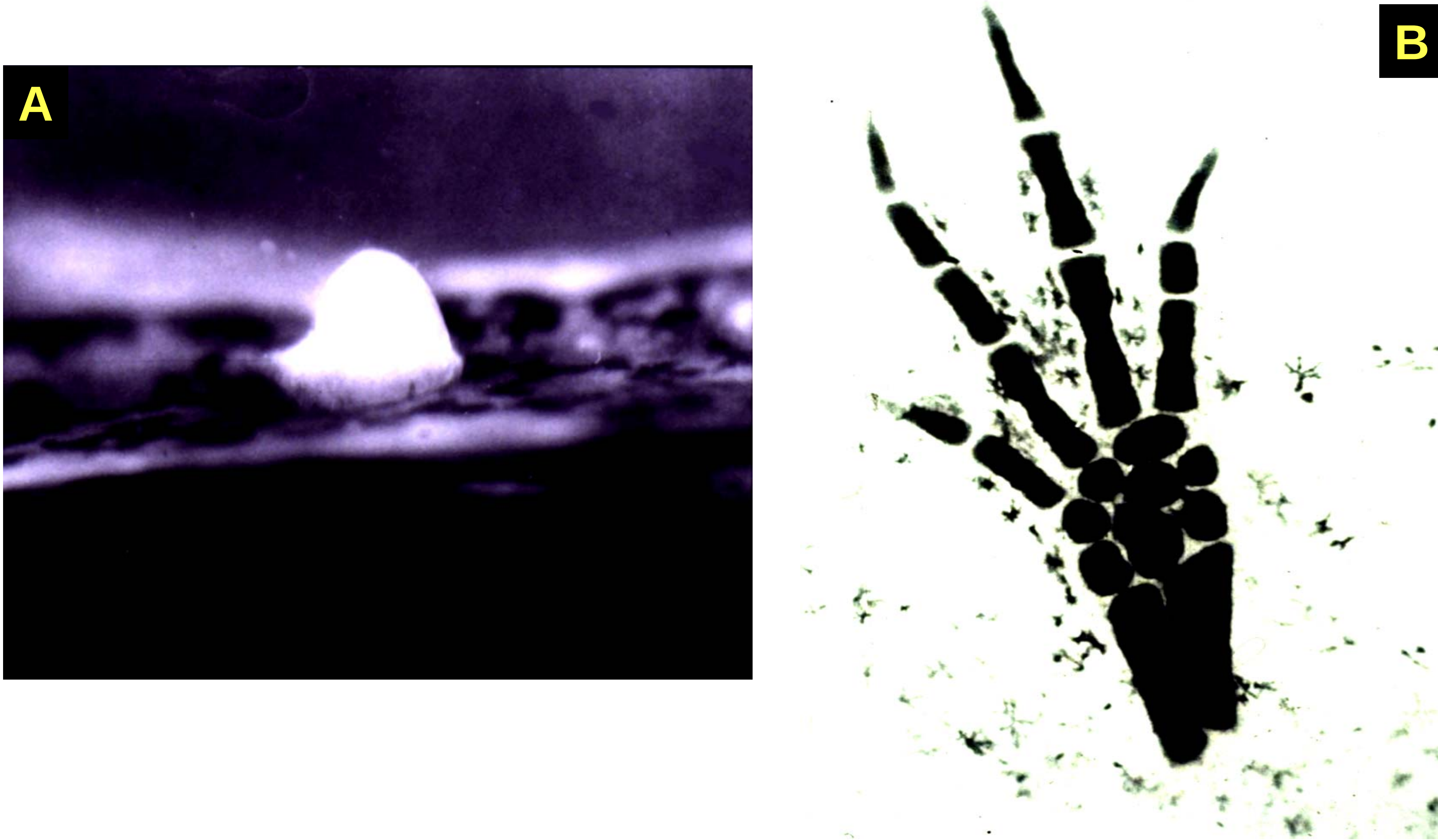
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PHYSICAL PROBLEMS THAT PRESENT THEMSELVES

COMPUTATIONAL ANALYSIS OF

- SHAPE CHANGES OF THE BLASTEMA AS IT FORMS, GROWS AND IS PATTERNED AND UNDERGOES MORPHOGENESIS INTO THE DIFFERENT LIMB SEGMENTS
- MITOSIS AND APOPTOSIS AS A FUNCTION OF LOCATION WITHIN THE BLASTEMA AND STAGE OF DEVELOPMENT
- PATTERN OF CELL DENSITY CHANGE AS THE BLASTEMA GROWS AND CHANGES SHAPE
- DIFFERENTIAL ADHESION AND CELL MOTILITY IN BLASTEMA FORMATION AND MORPHOGENESIS
- MORPHOGEN GRADIENTS
- GENE ACTIVITY NETWORKS
- SIZE-RELATED PHYSICAL/GEOMETRICAL CONSTRAINTS ON REGENERATION

MAPPING OF THE BLASTEMA: WHAT PARTS CONTRIBUTE TO WHAT STRUCTURES? NEW IMAGING TECHNIQUES?

ADHESION

ELSEVIER

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PHYSICA A

Physica A ■ (■■■■) ■■■–■■■

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Adhesion between cells, diffusion of growth factors, and elasticity of the AER produce the paddle shape of the chick limb

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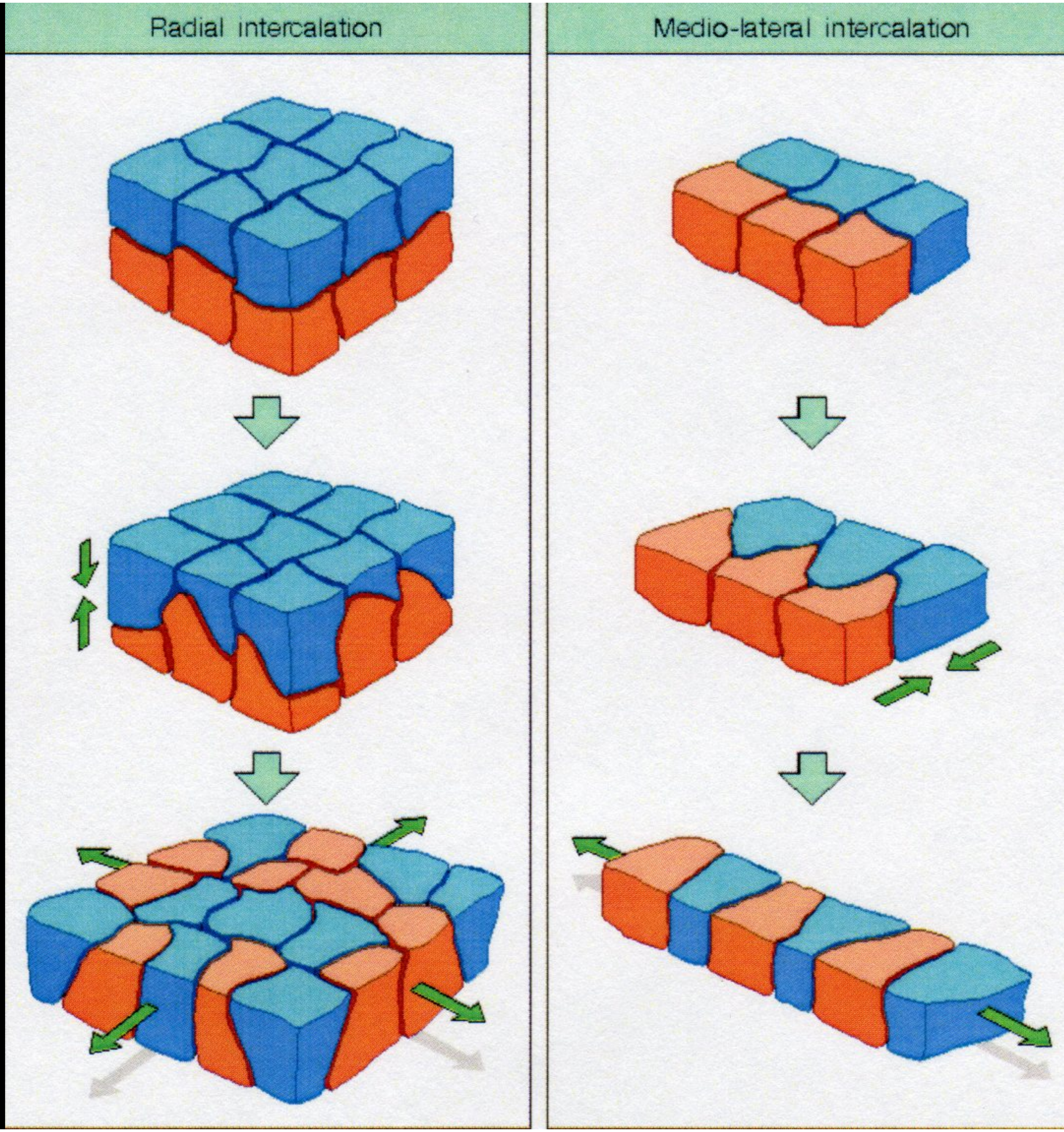
Biocomplexity Institute and Department of Physics, Indiana University, 727 East Third Street, Swain Hall West 117, Bloomington, IN 47405-7105, USA

Received 9 January 2006

Abstract

A central question in developmental biology is how cells interact to organize into tissues? In this paper, we study the role of mesenchyme-ectoderm interaction in the growing chick limb bud using Glazier and Graner's cellular Potts model, a grid-based stochastic framework designed to simulate cell interactions and movement. We simulate cellular mechanisms including cell adhesion, growth, and division and diffusion of morphogens, to show that differential adhesion between the cells, diffusion of growth factors through the extracellular matrix, and the elastic properties of the apical ectodermal ridge together can produce the proper shape of the limb bud.

Keywords: Cellular Potts model; Cell adhesion; Chick limb growth; Apical ectodermal ridge; Fibroblast growth factor; CompuCell3D


Radial intercalation
Medio-lateral intercalation

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Simulating convergent extension by way of anisotropic differential adhesion

Mark Zajac[a,*], Gerald L. Jones[a], James A. Glazier[b]

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Received 27 June 2002; accepted 12 December 2002

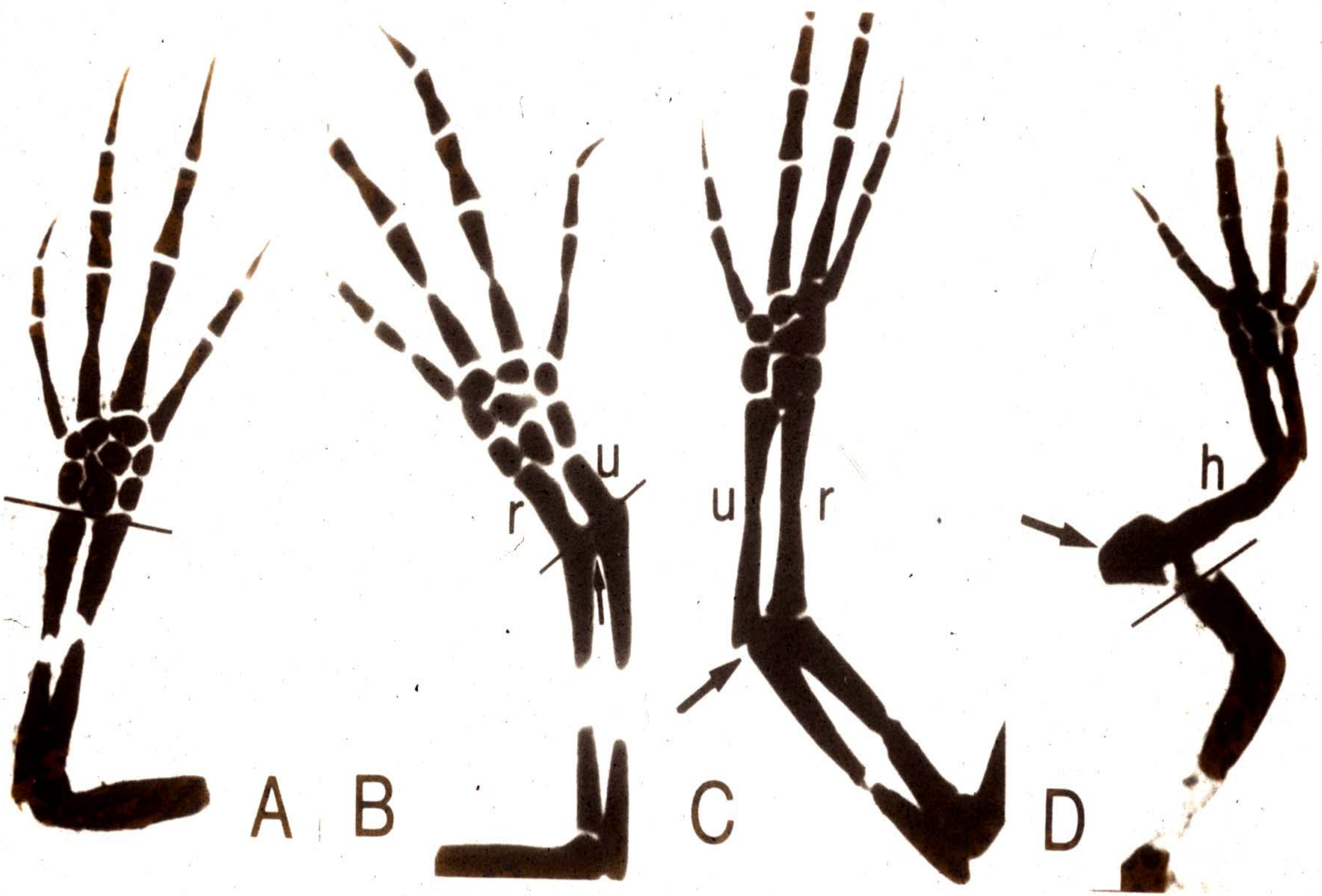
Abstract

Simulations using the Extended Potts Model suggest that anisotropic differential adhesion can account for convergent extension, as observed during embryonic development of the frog *Xenopus laevis* for example. During gastrulation in these frogs, convergent extension produces longitudinal tissue growth from latitudinal elongation and migration of aligned constituent cells. The Extended Potts Model employs clustered points on a grid to represent subdivided cells with probabilistic displacement of cell boundaries such that small changes in energy drive gradual tissue development. For modeling convergent extension, simulations include anisotropic differential adhesion: the degree of attachment between adjacent elongated cells depends on their relative orientation. Without considering additional mechanisms, simulations based on anisotropic differential adhesion reproduce the hallmark stages of convergent extension in the correct sequence, with random fluctuations as sufficient impetus for cell reorganization.

Keywords: Convergent extension; Differential adhesion; Computer simulations; Energy minimization

PROXIMODISTAL GRADIENTS OF CELL ADHESION EXIST IN REGENERATING LIMBS

RETINOIC ACID COORDINATELY PROXIMALIZES BLASTEMA CELL POSITIONAL IDENTITY AND CELL ADHESION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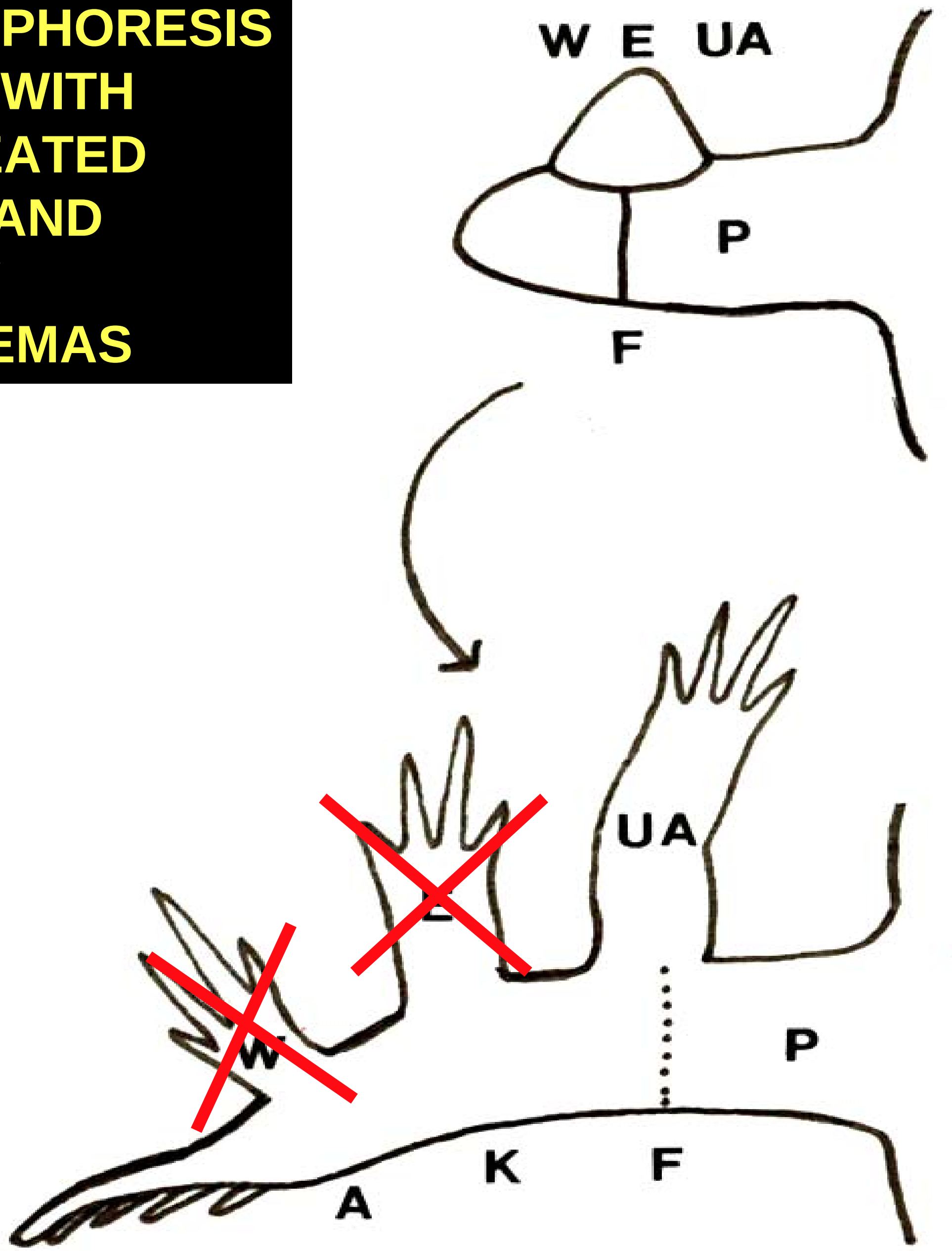
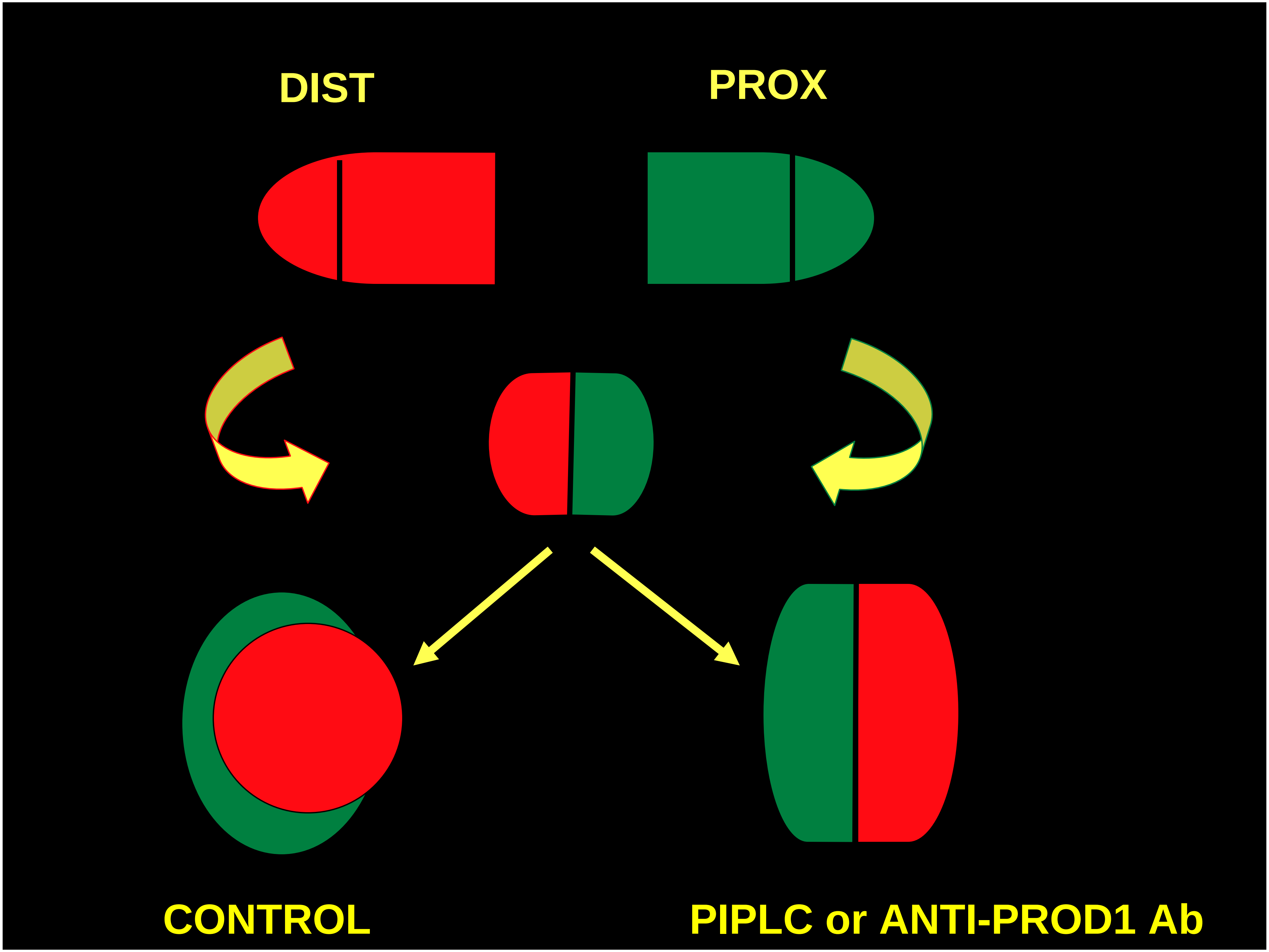
AFFINOPHORESIS ASSAY WITH RA-TREATED WRIST AND ELBOW BLASTEMAS

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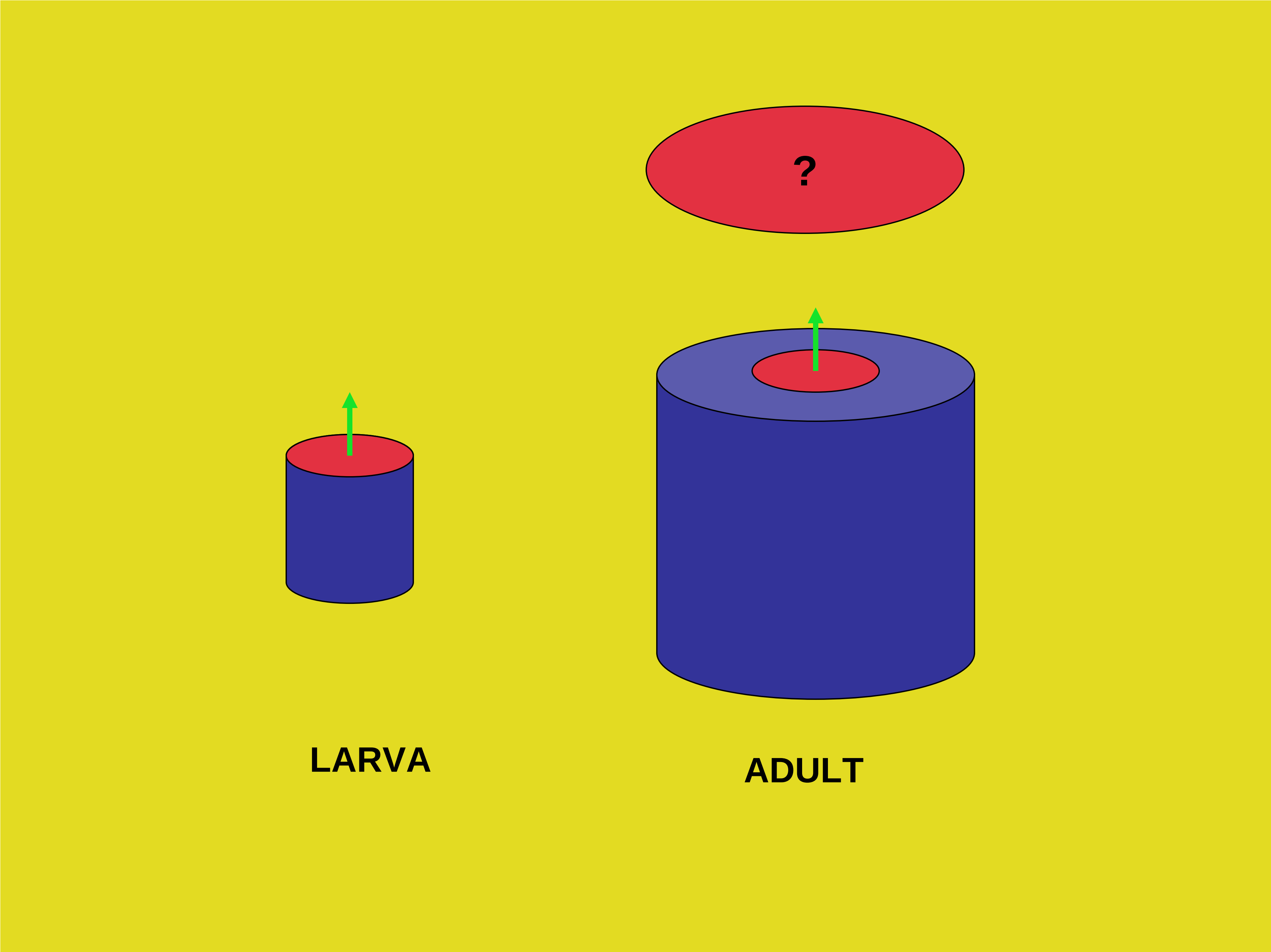
POSITIONAL IDENTITY IS ENCODED IN THE CELL SURFACE AND CELLS DETECT DISCONTINUITIES BY CELL SURFACE INTERACTION

PHYSICAL CONSTRAINTS


?
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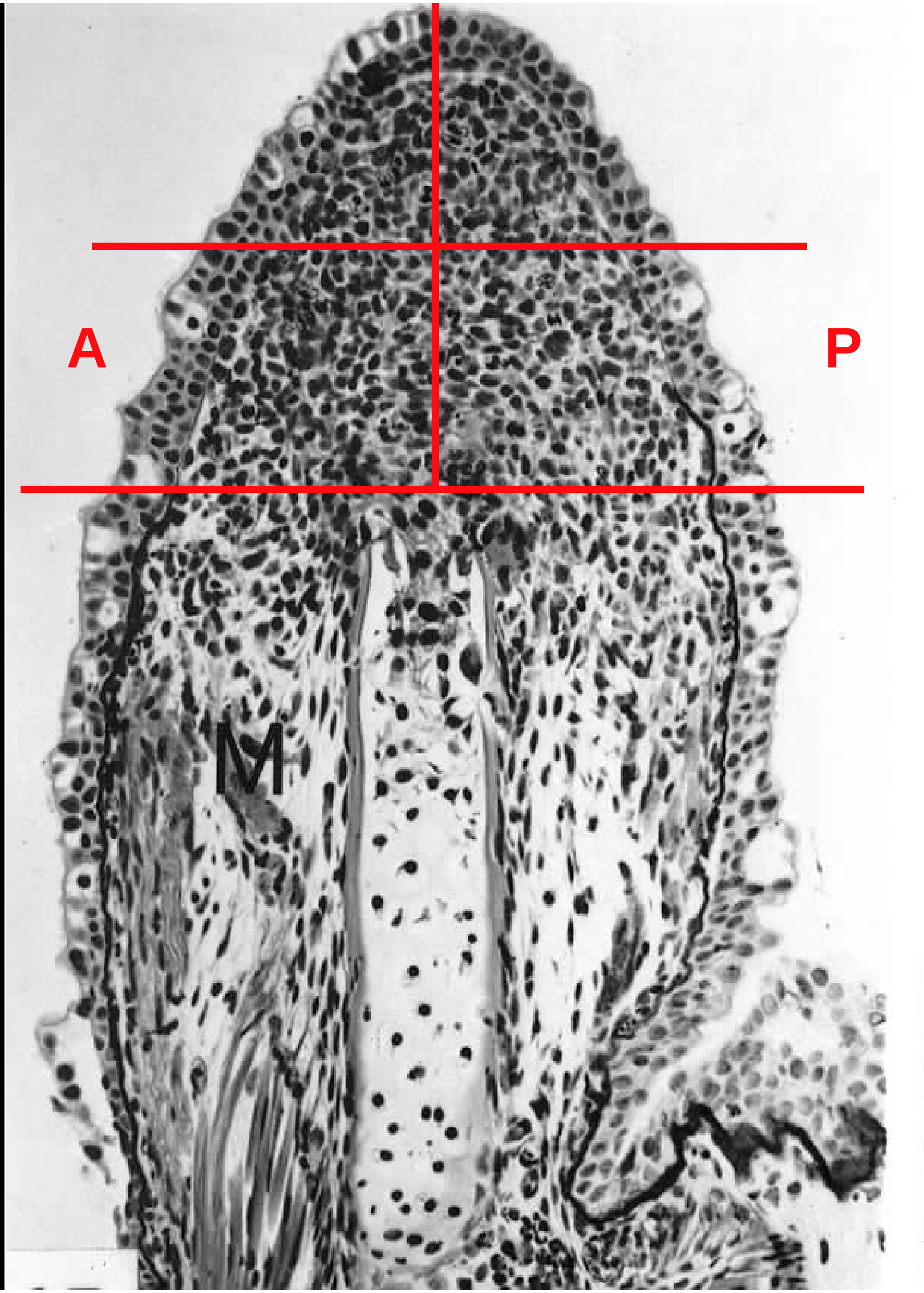
ADULT

MAPPING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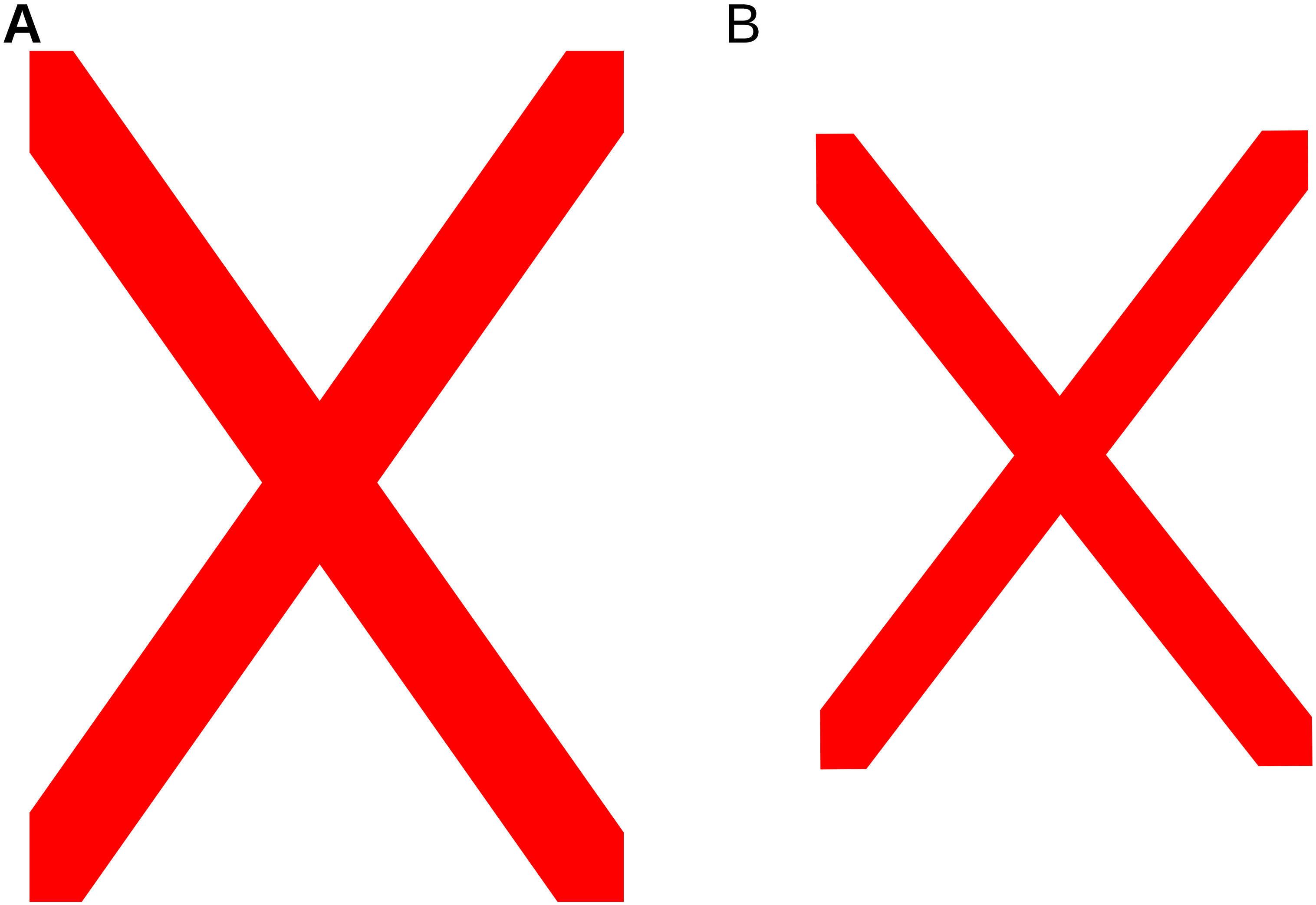
A
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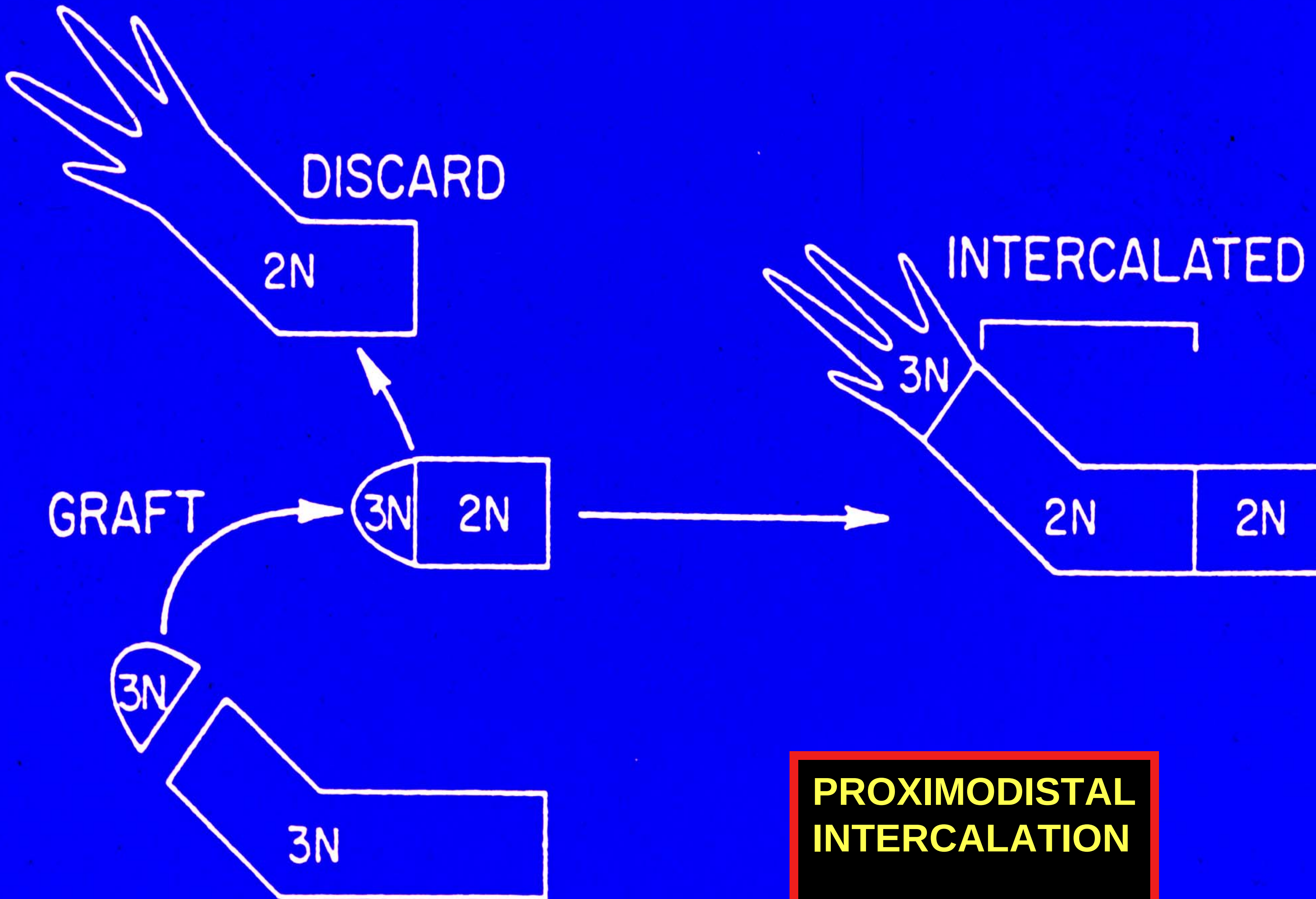
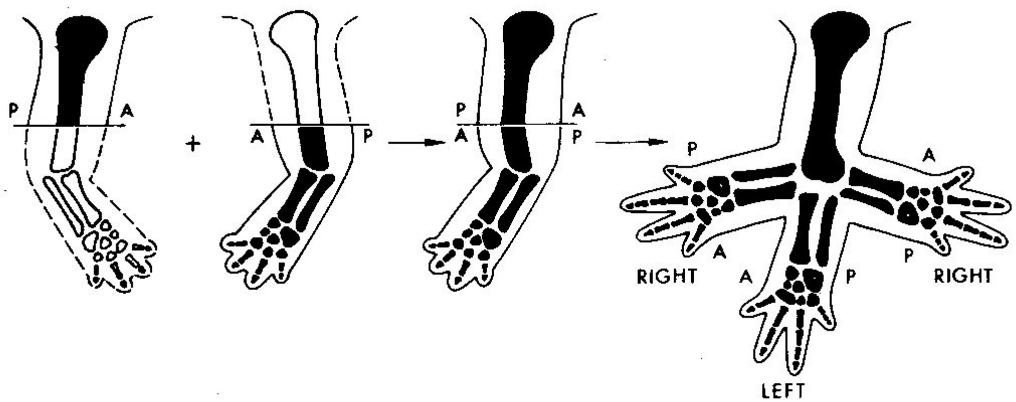
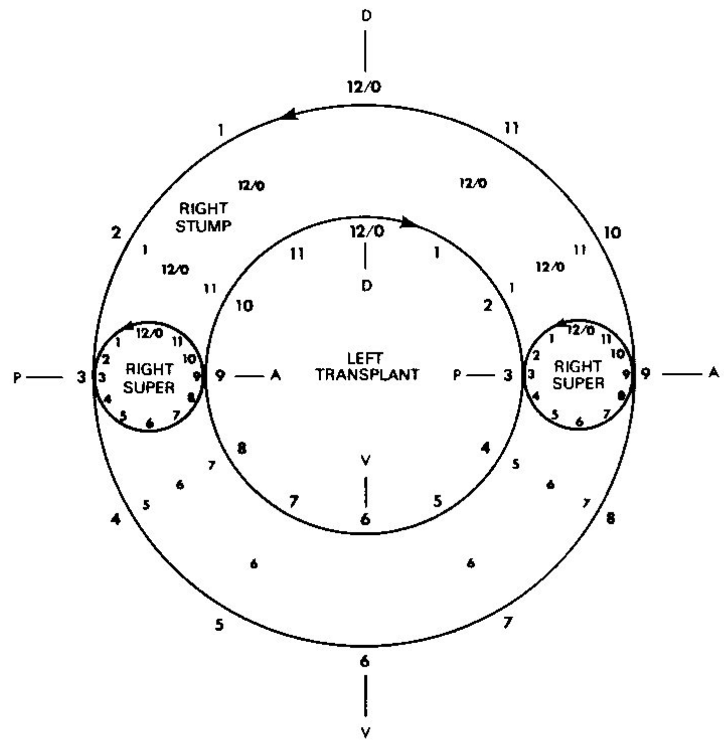
THE ROLE OF INTERCALATION IN REGENERATING STRUCTURE



PROXIMODISTAL INTERCALATION

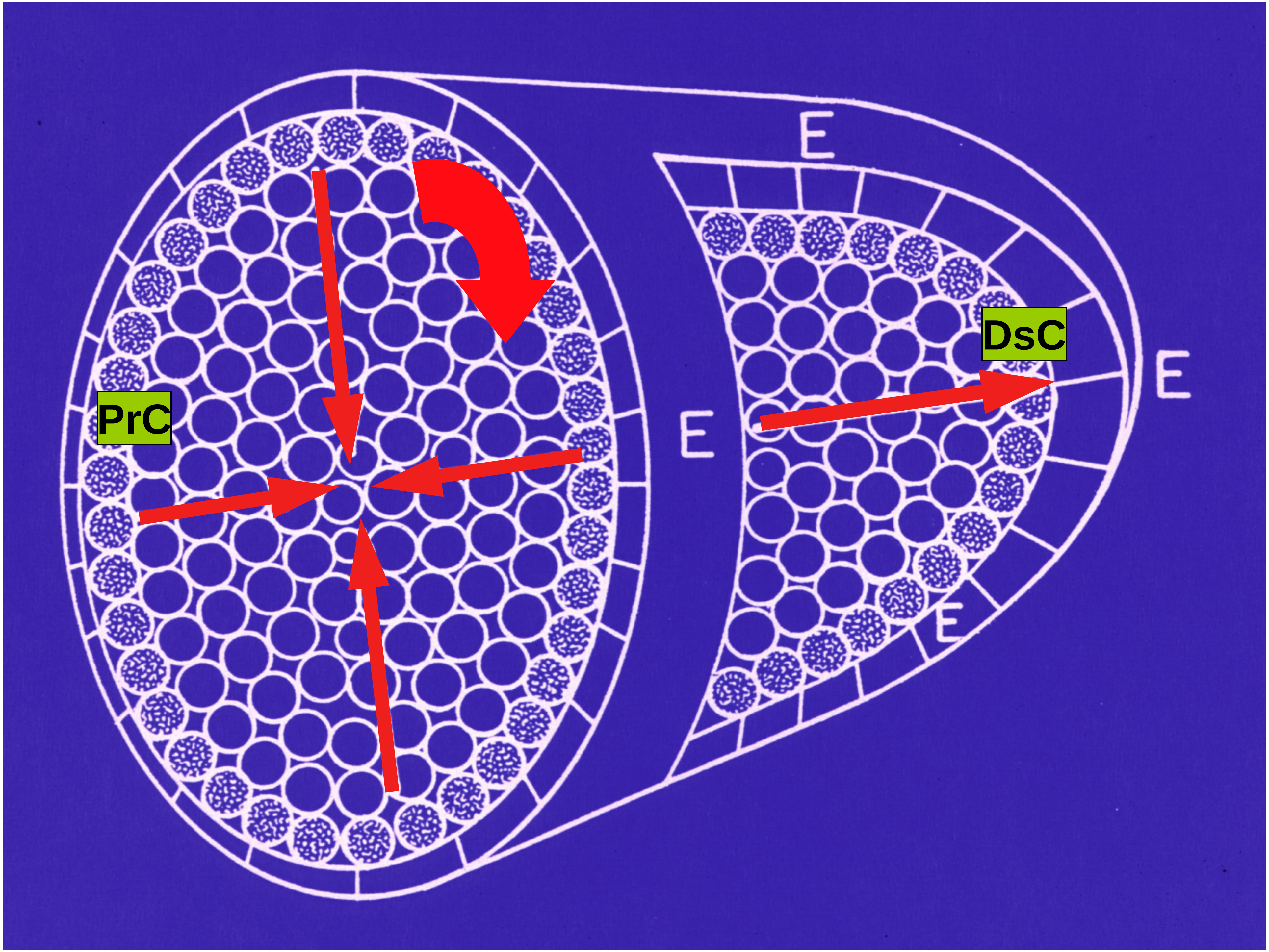
CIRCUMFERENTIAL INTERCALATION





REVERSAL OF THE ANTERIOR-POSTERIOR AXIS: CONTRALATERAL GRAFT

BOUNDARY MODEL FOR SELF-ORGANIZATION BASED ON INTERCALARY REGENERATION OF CELLULAR POSITIONAL IDENTITIES



E
E
E
E
PrC
DsC

LEAST THINGS

FERMAT'S PRINCIPLE OF LEAST TIME

In going from point A to point B, light takes the path that that requires the shortest time.

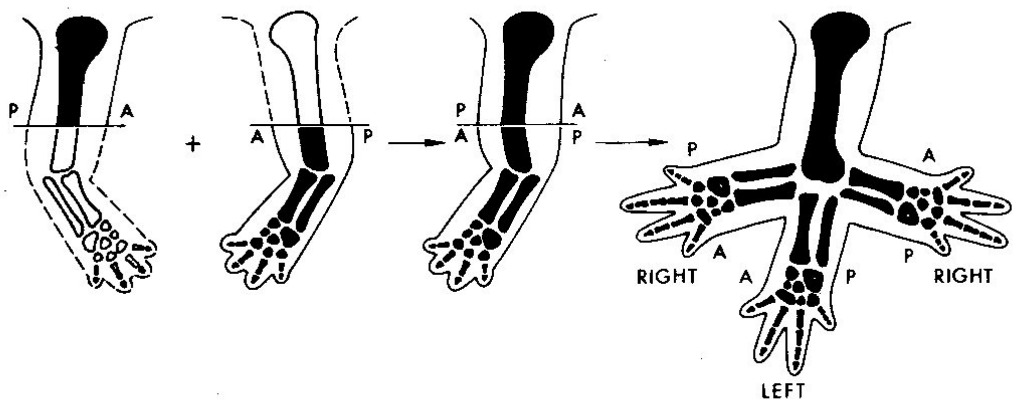
PRINCIPLE OF LEAST ACTION

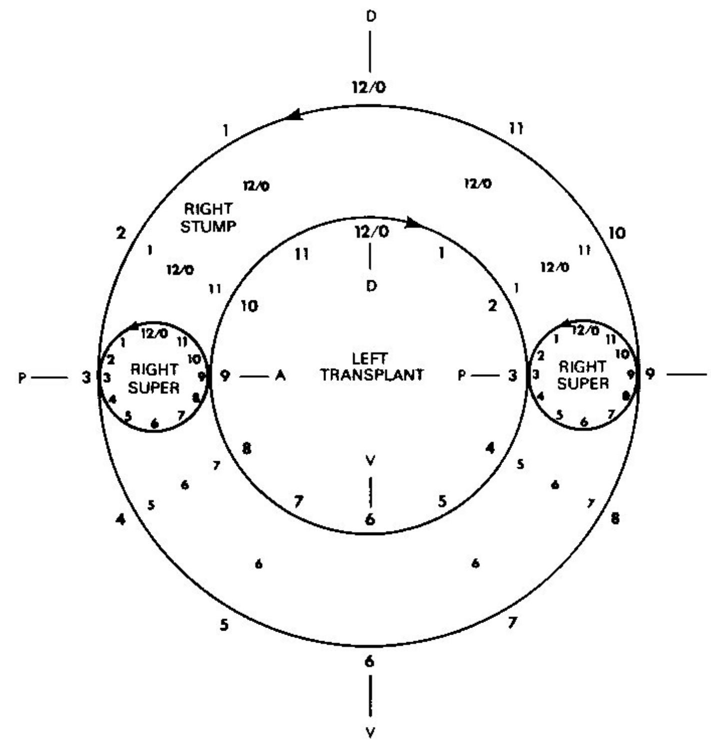
The path of an object or particle from point A to point B is the path for which the kinetic energy minus the potential energy Is the least

RULE OF LEAST (SHORTEST) INTERCALATION

Given a choice between the longer path or the shorter path to eliminate a positional discontinuity, cells always choose the shorter path.

3 4 5 6 7 8 9 10 11 12 1 2 3 OR THE REVERSE





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- RESEARCH GROUPS

  --CENTER FOR REGENERATIVE BIOLOGY AND MEDICINE, IUPUI

  --REGENERATION AND TISSUE ENNGINEERING THEME, INSTITUTE FOR GENOMIC BIOLOGY, UIUC

INDIANA UNIVERSITY CENTER FOR REGENERATIVE BIOLOGY AND MEDICINE

INDIANA UNIVERSITY - PURDUE UNIVERSITY INDIANAPOLIS

MISSIONS: MULTIDISCIPLINARY RESEARCH, ACADEMIC TRAINING, TECHNOLOGY TRANSFER

PARTICIPATING UNITS

- SCHOOL OF SCIENCE (Founder & Administrative Unit)
- SCHOOL OF MEDICINE

CONTACTS

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Regeneration

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