**November 2, 2016 The Nardi-Stocum Phenomenon** of limb regeneration.

**Displacement of grafted limb tissue along its proximo-distal axis.**

When elbow cells get grafted to the hand (or to the shoulder)

the grafted cells somehow move back to the elbow position.

*Also:* ***Hand cells get engulfed by elbow cell***s,

 **elbow cells get engulfed by shoulder cells. etc.**

Similar to the engulfment of mesoderm cells by ectoderm, engulfment of heart by liver.

From which **N&S concluded the cause is what Steinberg had hypothesized**,

which is thermodynamic (surface tension-like) **maximization of cell-cell adhesions**.

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 **Retinoic acid causes big changes in behaviors of embryonic tissues:**

"Retinoic acid coordinately proximalizes regenerate patterns and blastema

differential affinity in axolotl limbs": K Crawford & DL Stocum Development 1988 cited by 93

"Use of retinoids to analyze the cellular basis of positionl memory in regenerating amphibian limbs,

DL Stocum and K Crawford Biochemistry and cell biology 1987 cited by 51

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***What is wrong with the following argument?***

Tissue engulfment looks like liquid surface tension: Surface tension is caused

by attractive forces pulling molecules toward each other; therefore tissue engulfment

must be driven by maximization of cell-cell adhesion:

& Cell adhesion should be measurable by resistance of cell aggregates to flattening.

When Nardi writes **"differential affinity"**, he means cell rearrangement behavior,

partly because he regards Steinberg's thermodynamic theory as being proven fact,

but also to avoid alternatives like: ***"That business with the bunches of cells engulfing each other."***

The less people understand about thermodynamics, the less they doubt such theories.

(A reason for biologists to take Physical Chemistry is future protection from bluffing.)

Imagine if someone claims "Quantum theory proves Warburg's theory about the cause of cancer"?

How can you argue with them? If you ask "How can you prove that?", what will they say?

My point is that ***even the best scientists can have trouble knowing what evidence proves.***

**All interpretations of data are attempts to fit observations to expectations, theories & guesses.**

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**All cases where cells gravitate back toward their original spatial arrangement**,

especially when the same end results can be reached by 2 or 3 or more pathways,

**get interpreted by many as thermodynamic minimization of free energy**.

An alternative explanation is homeostasis by negative feedback cycles.

Imagine if some persuasive person had argued that constant body temperature is caused by

minimization of thermodynamic free energy.