THE PHYSICS AND PATHOLOGY OF WOUNDS

3

CHRONICITY AND THE PHYSICS OF WOUND FAILURE

1

The Wound as a System and a Controlled Machine

2

Auto-Immunopathy and the Intrinsic Disease of Wound Healing

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THE PHYSICS AND PATHOLOGY OF WOUNDS

COMPARE WOUND STRUCTURE AND FUNCTION TO OTHER ORGANS

What are the quintessential structures and functions of these organs ?
What is the quintessence of dysfunction for these organs?
What are the fundamental physics relevant to these organs ?

ORGAN	STRUCTURE & FUNCTION	FAILURE	PHYSICS
HEART	*pump, valves, & pipes*	*chf = inadequate pump*	*fluid mechanics*
KIDNEY	*filter & resorption membrane*	*occluded filter*	*hydraulics & ionic chemistry*
LUNG	*bellows & diffusion membrane*	*faulty ventilation & respiration*	*gases & diffusion*
EYE	*light collector & detector*	*blindness*	*optics*
EAR	*sound transducer & decoder*	*deafness*	*acoustics*
BONE	*structural members & motion*	*impaired support & mobility*	*mechanics*
NERVES	*electrical network & control*	*open circuit neurologic deficits*	*electricity*
WOUND	*cell set & sel[illegible]nization* ? ? ?	*logistical di[illegible]tion* ? ? ?	*populations, [illegible]s, automata* ? ? ?

THE WOUND MODULE IS A SPECIAL AD HOC RESERVE ORGAN.

What are the quintessential structures and functions of the wound ?

What is the quintessential derangement of intrinsic wound pathology and chronicity?

What are the fundamental physics relevant to the wound ?

THE PHYSICS AND PATHOLOGY OF WOUNDS

COMPARE WOUND STRUCTURE AND FUNCTION TO OTHER ORGANS

What is the quintessence of these organs, and what is their fundamental physics ?

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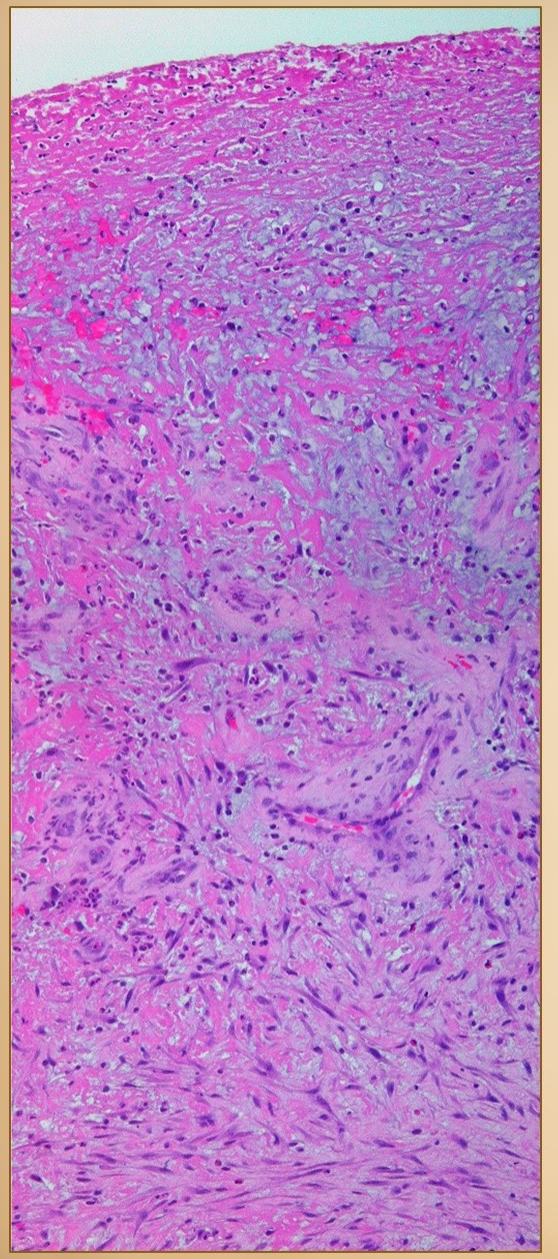
NERVES	*electrical network & control*	*open circuit neurologic deficits*	*electricity*
WOUND	*cell set & self-re-organization*	*logistical disorganization*	*populations, dynamics, automata*

THE WOUND MODULE IS A SPECIAL AD HOC RESERVE ORGAN

What are the quintessential structures and functions of the wound ?
It is a collection of mutually interactive self-organizing cell populations.

What is the quintessential derangement of intrinsic wound pathology and chronicity ?
It is a dynamical disorder of logistical self-re-organization among these populations.

What are the fundamental physics relevant to the wound ?
Non-linear dynamics, control, chaos, population logistics, cellular automata.



THE WOUND MODULE

OF PROLIFERATIVE REPAIR

and the

PHYSIOLOGIC EVENTS - CLINICAL SIGNS

0
injury
inflammation

1
inflammation
subsides

2
macrophages,
eschar separation,
cytokines

3
ground substance,
mucus

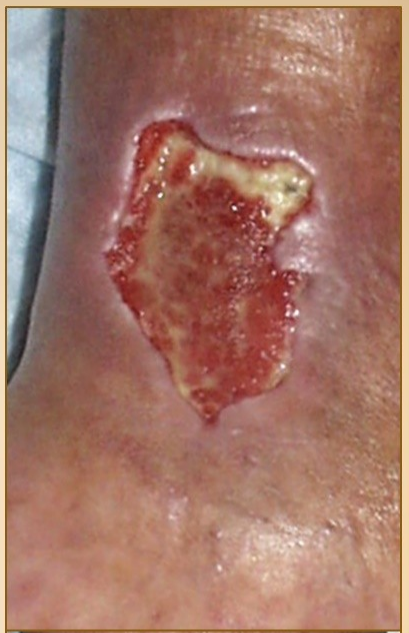
4
"granulation"
angiogenesis

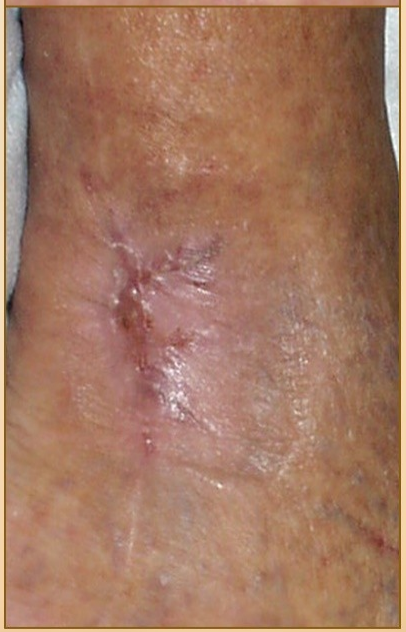
5
histioblasts, fibroblasts,
fibroplasia

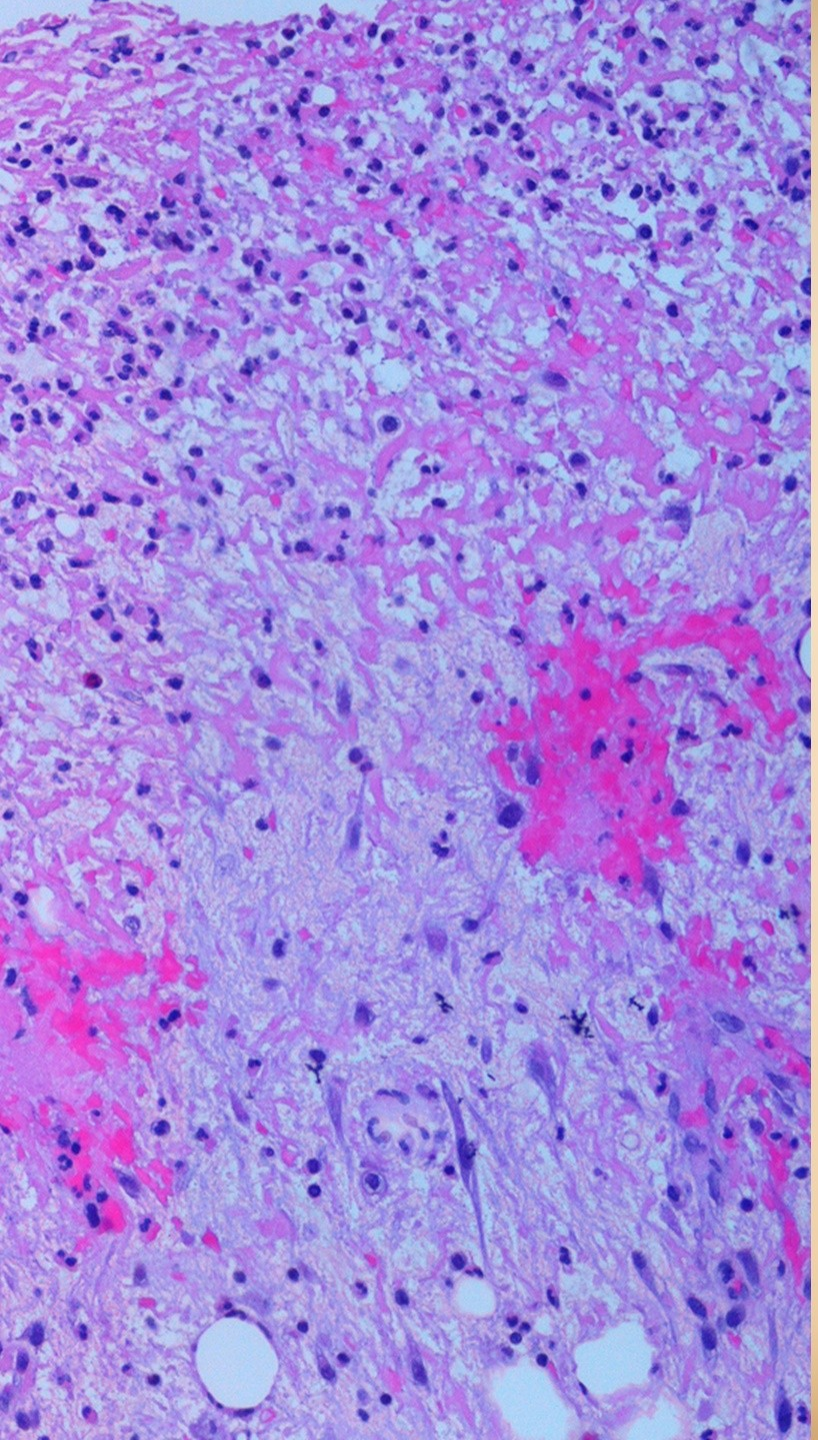
6
myofibroblasts
contraction

7
epithelialization

8
maturation







THE WOUND MODULE - NORMAL WOUND HEALING

MAIN EVENTS AND CELLS:

INFLAMMATION
(BLOOD BORNE CELLS)
Platelets
PMN leukocytes
(Granular leukocytes) *(No lymphoid cells)*

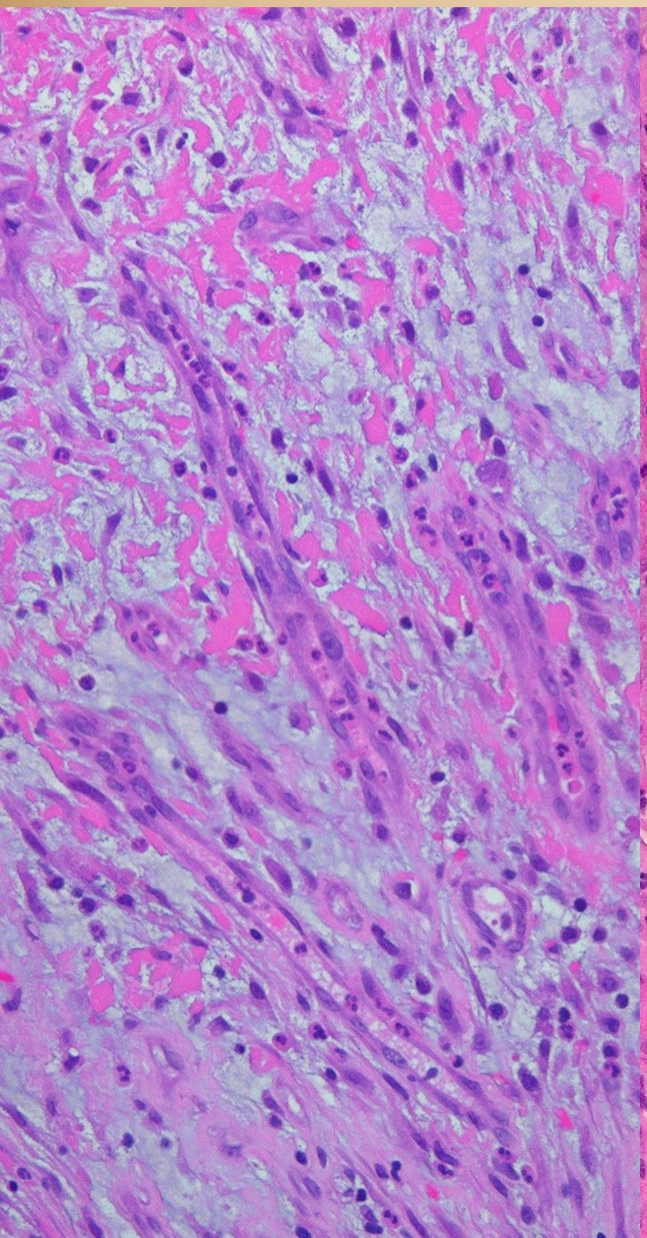
AFFERENT WOUND EVENTS
(TRANSFORMED CELLS)
Macrophages

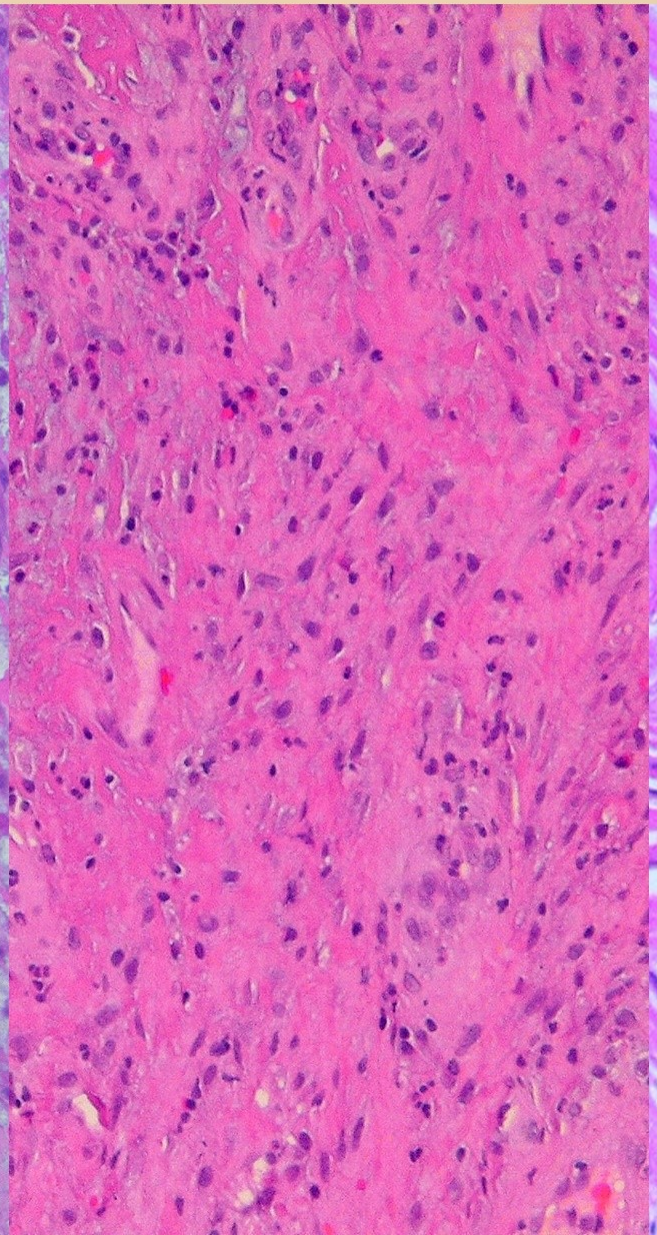
MESENCHYMAL REPAIR
(LOCAL CELLS)
2 cells:
Angiocytes & Fibroblasts

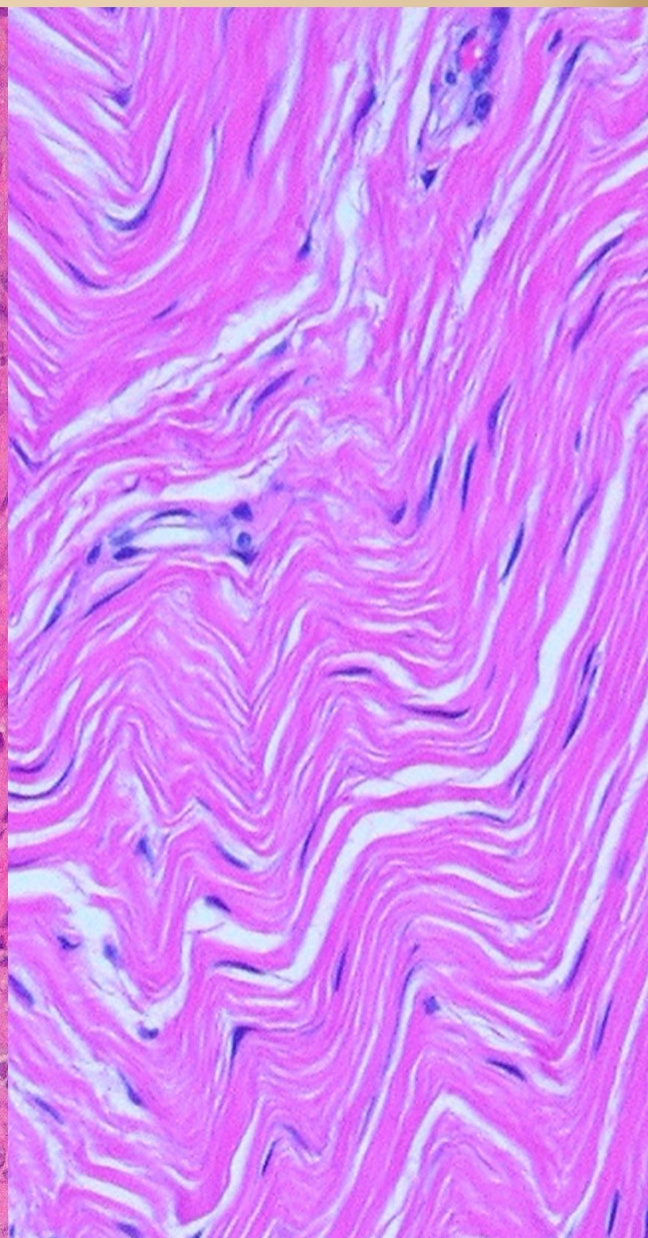
SEQUESTRATION
(LOCAL CELLS)
Epithelium

RESTORATION OF STROMA

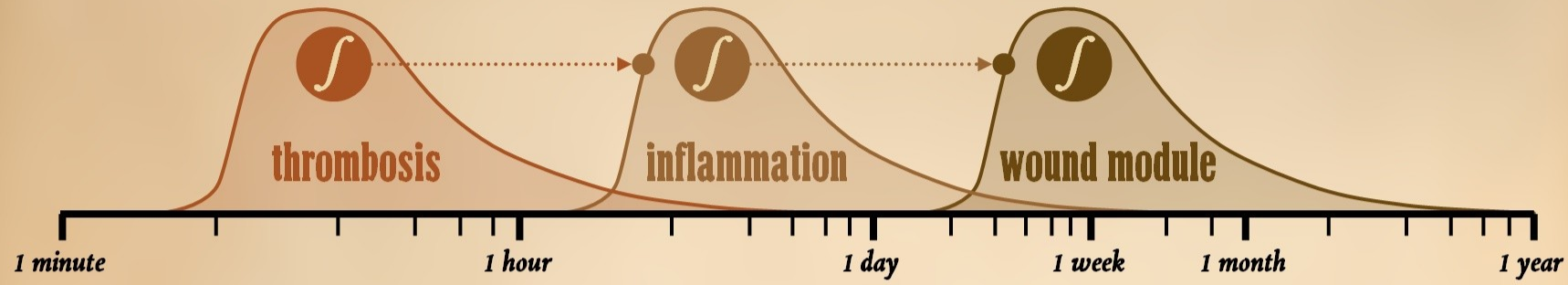
REPAIR IS BASED ON 2 CELL TYPES - ANGIOCYTES & FIBROBLASTS



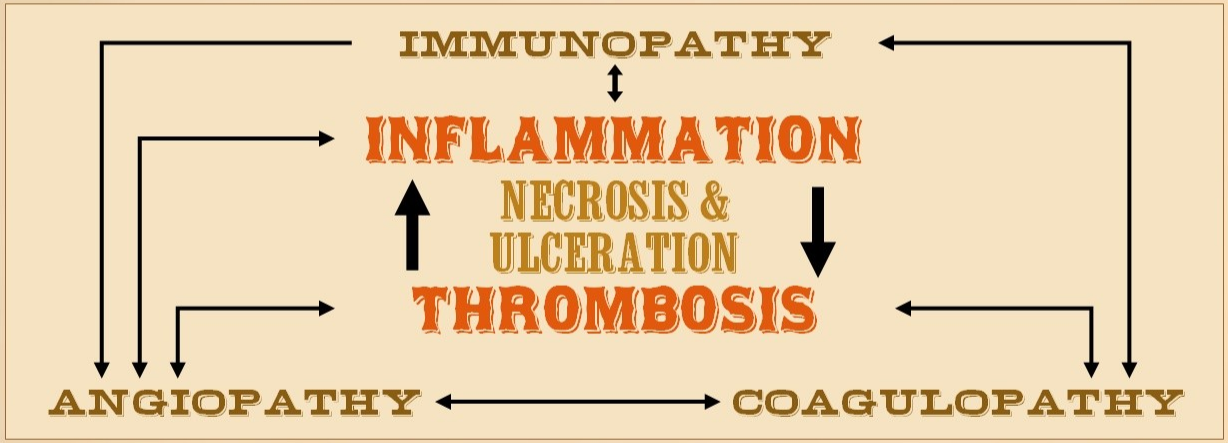




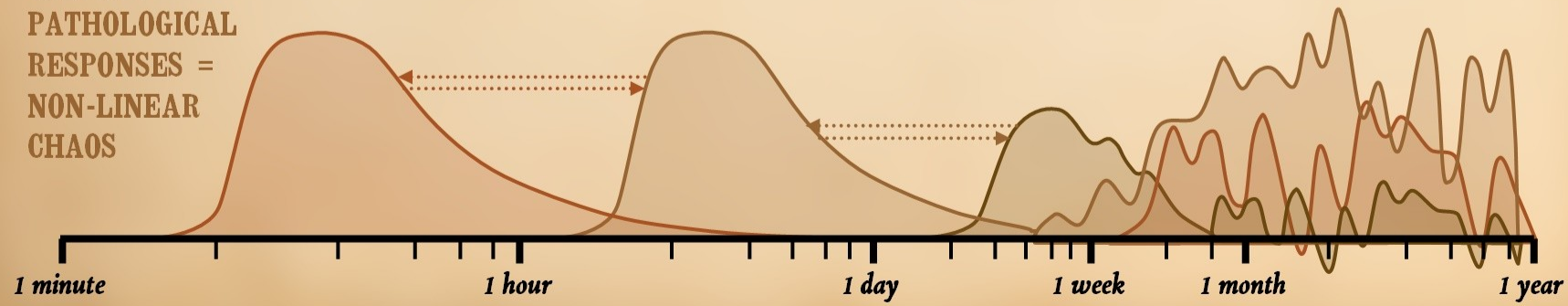
INTER-CONNECTIONS



NORMAL HEALTHY RESPONSES = SEQUENTIAL LINEAR ONE-SHOTS



CHRONIC PATHOLOGICAL RESPONSES = NON-LINEAR CHAOS



THE PHYSICS AND PATHOLOGY OF WOUNDS

THE WOUND MODULE IS A SPECIAL AD HOC RESERVE ORGAN

It is a collection of mutually interactive self-organizing cell populations.

The wound is not a pump and pipes like the heart,
not a diffusion membrane like the lung,
not a structural member like a bone,
not a light collector like the eye,
not like any other already organized organ with a specific task to do.
It is a collection of mutually interactive self-organizing cell populations.
It has no other function than to get organized
(into a generic stroma that is the foundation for other tissues and organs.)

Wound failure is a dynamical disorder of logistical self-re-organization among these populations.

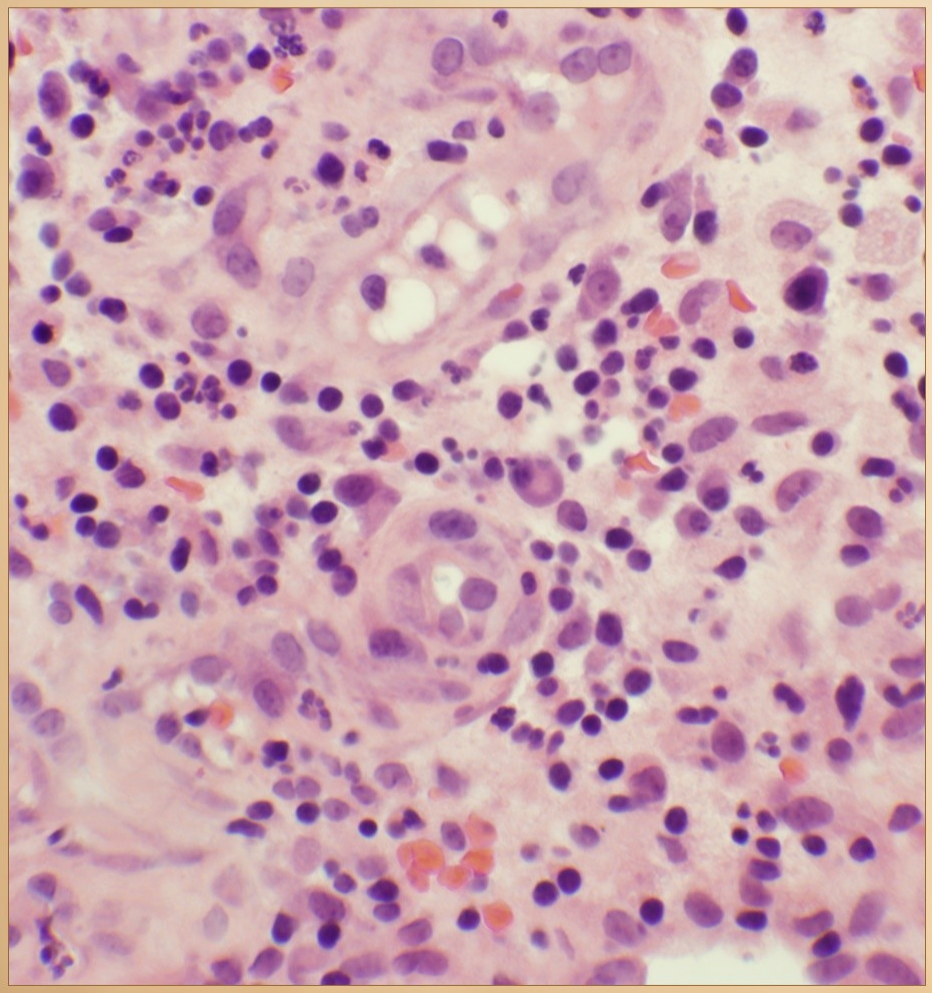
When it fails, it is not an inadequate pump like the heart,
not an inadequate filter like the kidney,
not an inadequate bellows or diffusion membrane like the lung,
not like any other organ that has something to do.
When it fails, it simply fails to get organized into its intended final form,
to complete its task to become something and then cease.

Non-linear dynamics, control, population logistics, cellular automata.

The relevant physics is not fluid dynamics like it is for the heart,
not optics like it is for the eye,
not acoustics like it is for the ear.
It is the science of populations and the principles of their interaction, control, and self-organization.
When it fails, it is, in the terms of its relevant physics, a dynamical disorder of self-organizing populations.

CHRONICITY & THE PATHOLOGY OF WOUND FAILURE

THE RELEVANT PHYSICS OF WOUND HEALING, NORMAL & FAILING



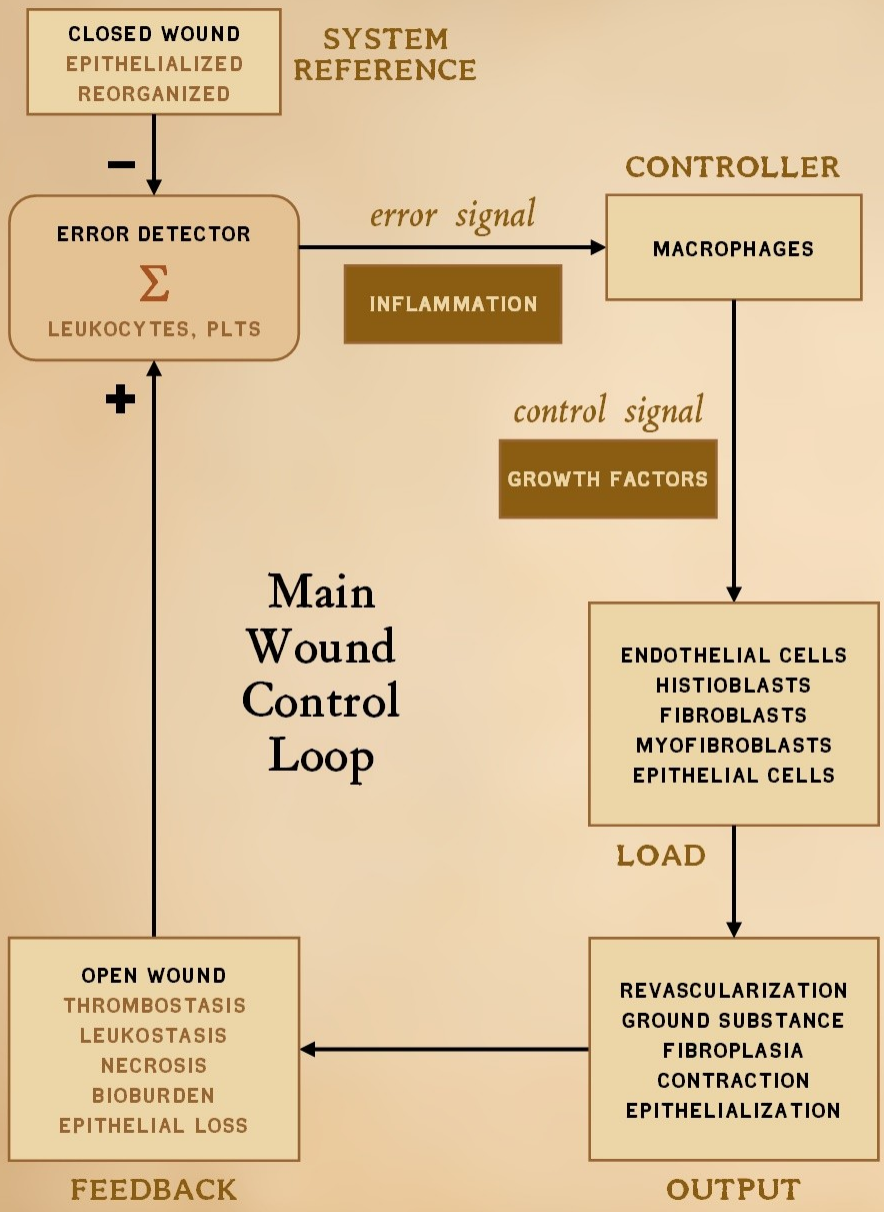
NON-LINEAR DYNAMICS

Control
Chaos
Attractors
N-Body Dynamics

Population Logistics

Cellular Automata
& Self-Organization

INTEGRATED WOUND PHYSICS



CHRONICITY AND THE PATHOLOGY OF WOUND FAILURE

THE RELEVANT PHYSICS OF IMPAIRED WOUND HEALING

NON-LINEAR DYNAMICS

Control

Chaos
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Population Logistics

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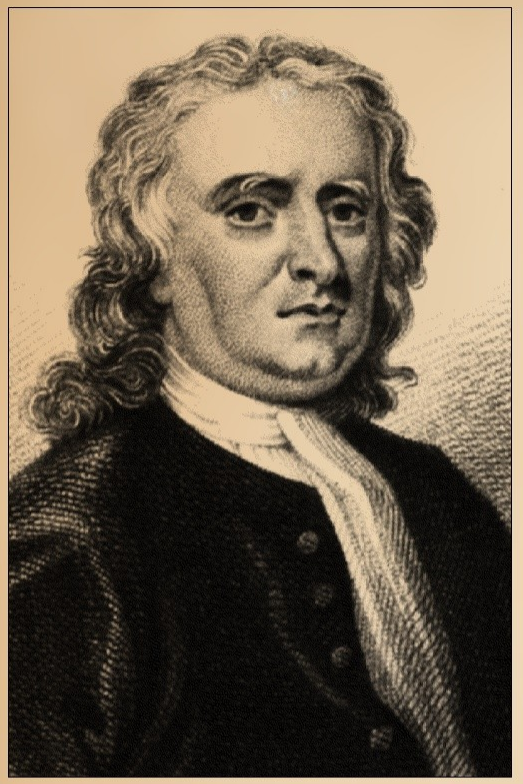
INTEGRATED WOUND PHYSICS



Isaac Newton
c 1700

Henri Poincaré
c 1900

Intractability and the 3-Body Problem

CHRONICITY AND THE PATHOLOGY OF WOUND FAILURE

THE RELEVANT PHYSICS OF IMPAIRED WOUND HEALING

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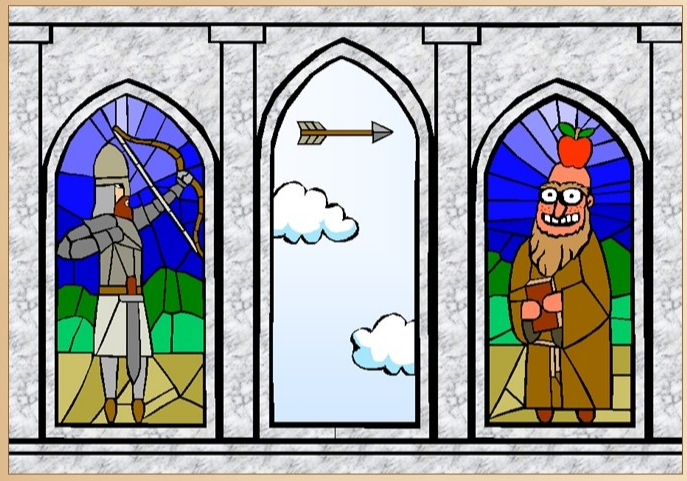
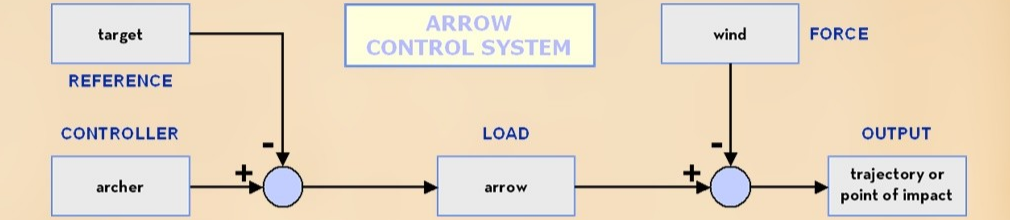
INTEGRATED WOUND PHYSICS

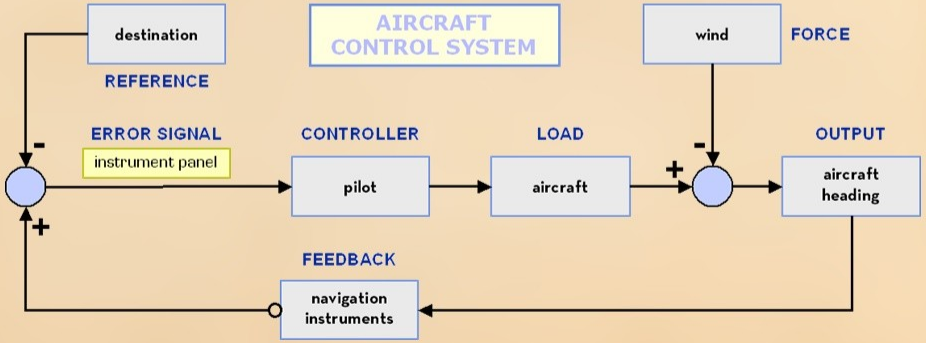
CONTROL & NON-LINEARITY - THE NEED FOR CONTROL

Control lets a system hold itself to a desired output, state, or attractor. Key to control is feedback, the ability to sense the system state or output, which then drives an error correcting mechanism.



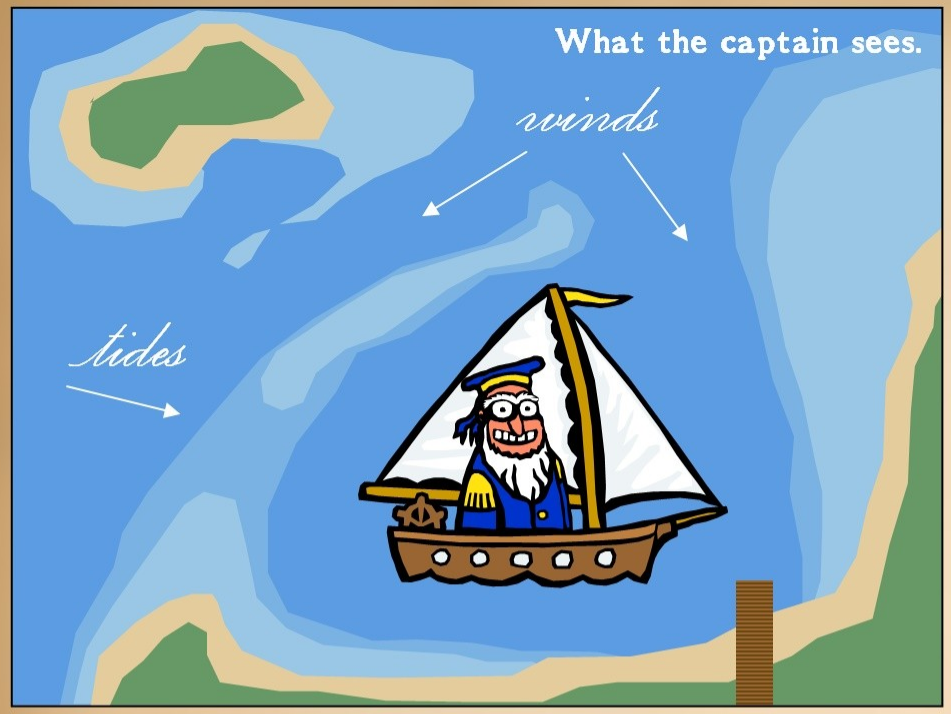


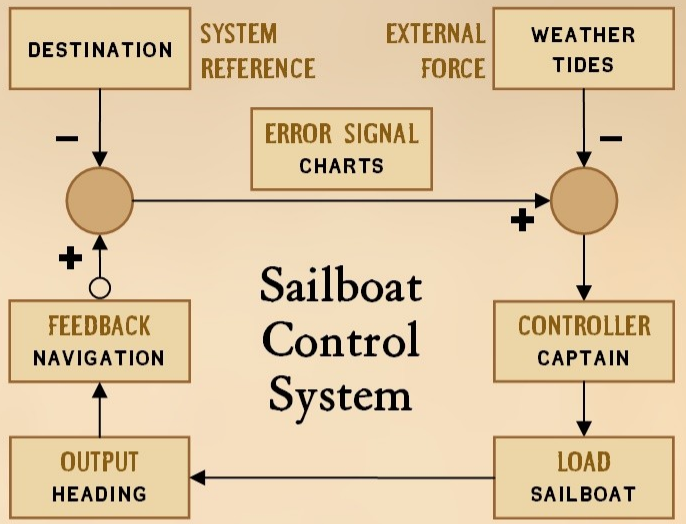
ARROW: No feedback - open loop. Course cannot be assessed nor corrected. Must be calibrated (aimed), and if a gust of wind or anything upsets that calibration, the system misses its mark.

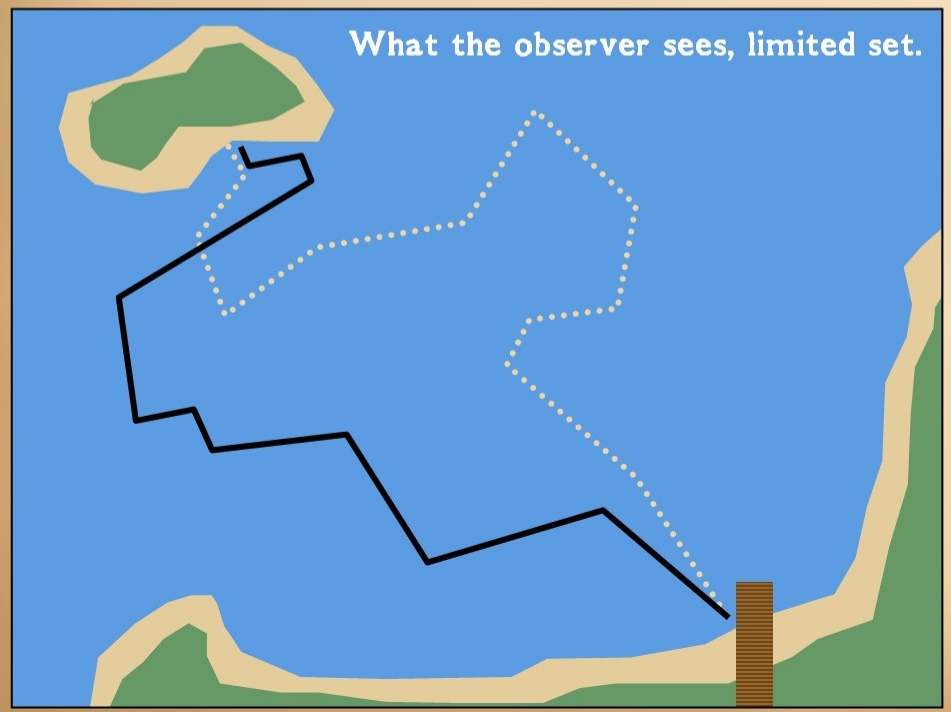


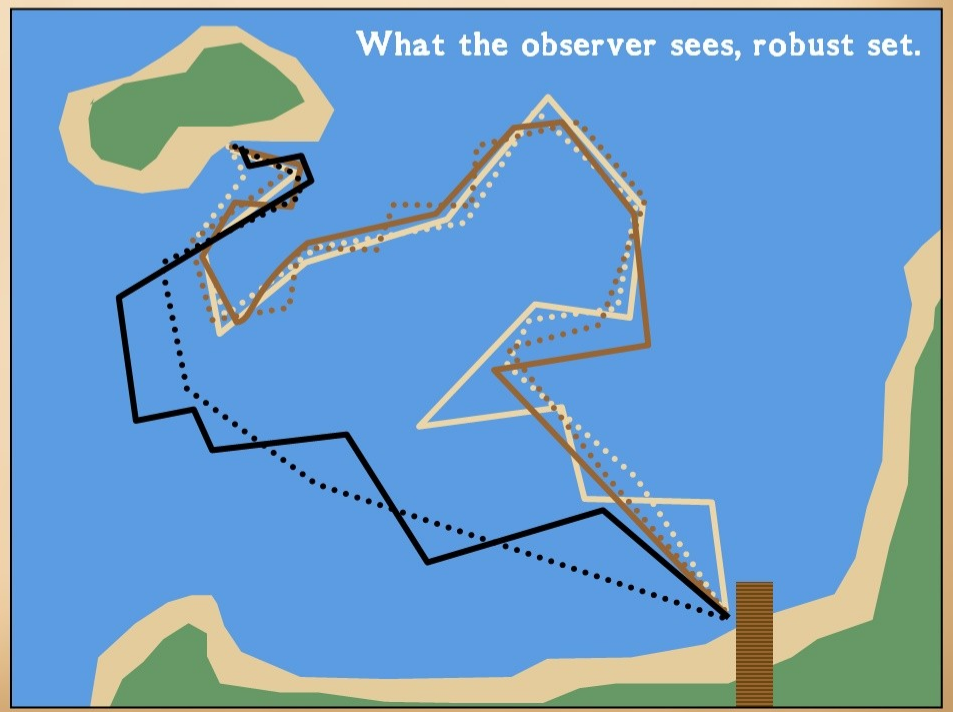
AIRPLANE: Steered, not aimed. Pilot and flight controls assess and correct the plane's heading. Feedback and closed loop control assure that system reaches target, even when perturbed.

A Demonstration of Chaos and Attractors







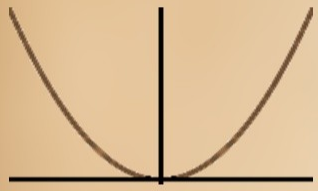


NON-LINEAR DYNAMICS & ITERATION

CHAOS - ATTRACTORS - COMPLEXITY

Iterate x2 , real

$$x \leftarrow x^2$$



Iterate $f(x) = x2$

START WITH ARBITRARY x.
SQUARE IT.
THIS IS THE NEXT x.
SQUARE IT AGAIN,
AND SO ON.

This system has 3 attractors. Each x will do 1 of 3 things:

for $|x_0| < 1$, $x \to 0$
for $|x_0| = 1$, $x_n = 1$
for $|x_0| > 1$, $x \to \infty$

Iterate x^2 , complex

$$x \leftarrow x^2 + c$$

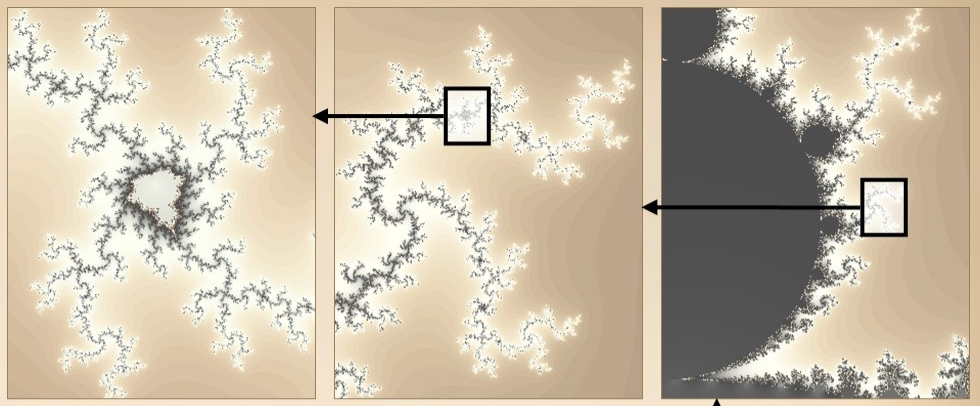
Assign sequential colors to each point / pixel based on the number of iterations to "blow up" or the number of iterations in each orbit.

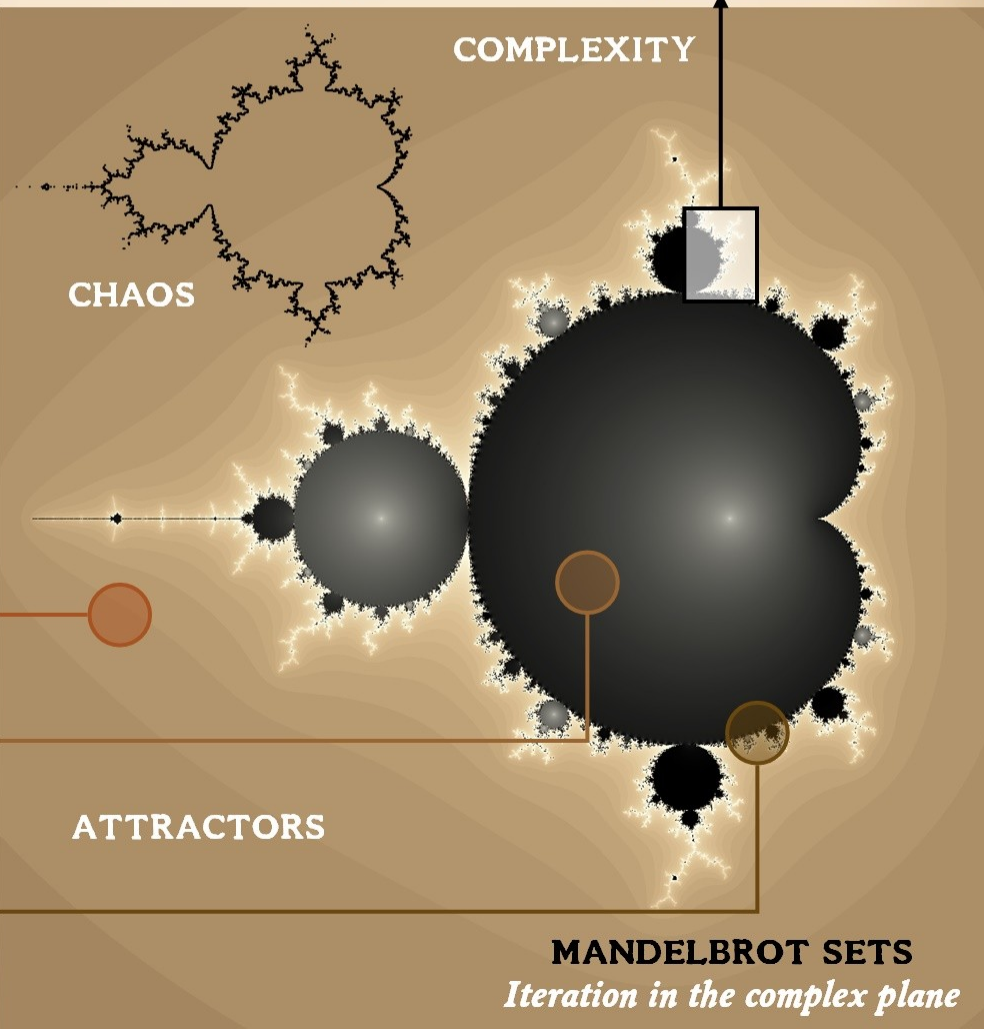
This system has three attractors. Each point in the complex c-plane will do one of three things:

It will diverge to infinity.

It will converge to a stable orbit of period *n*.

It will neither converge nor diverge, locked in an orbit of infinite period.

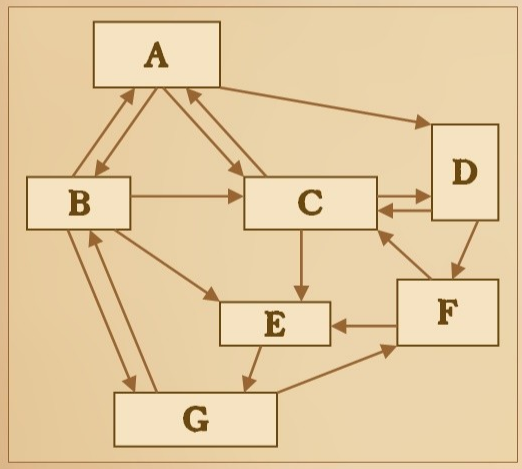


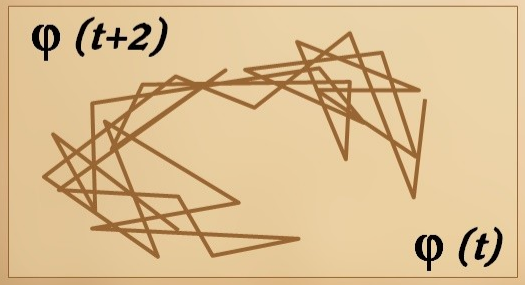


MANDELBROT SETS
Iteration in the complex plane

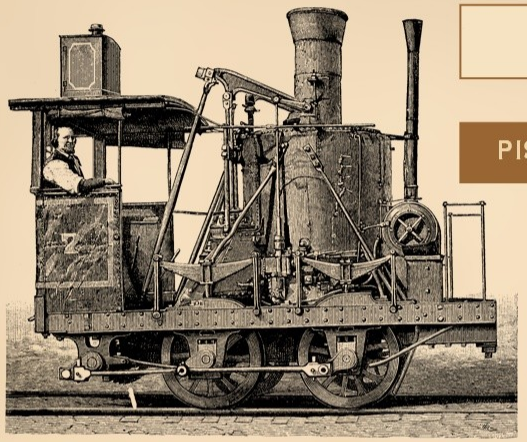
NON-LINEAR DYNAMICS & ITERATION : N-BODY PROBLEMS & MULTI-CONTROL

N-body & Non-linearity





Example: flow = rate x volume (φ = r × v)



A linear system

PISTON RATE — STROKE VOLUME

$$d\varphi = v\,\partial r + r\,\partial v$$
$$\partial\varphi = v\,\partial r$$
$$\partial\varphi = r\,\partial v$$

PUMP OUTPUT

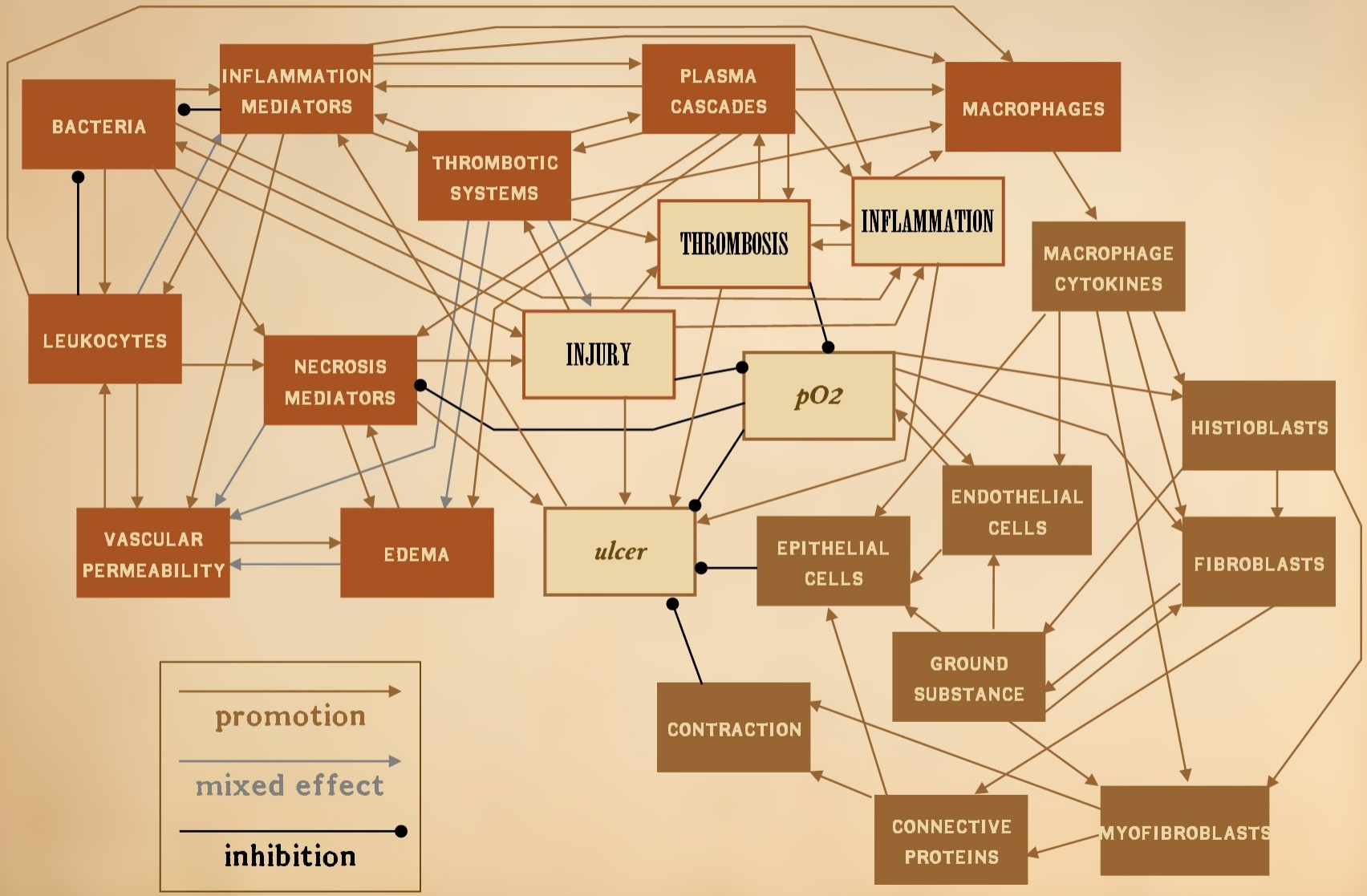
A non-linear system

HEART RATE ⇄ STROKE VOLUME

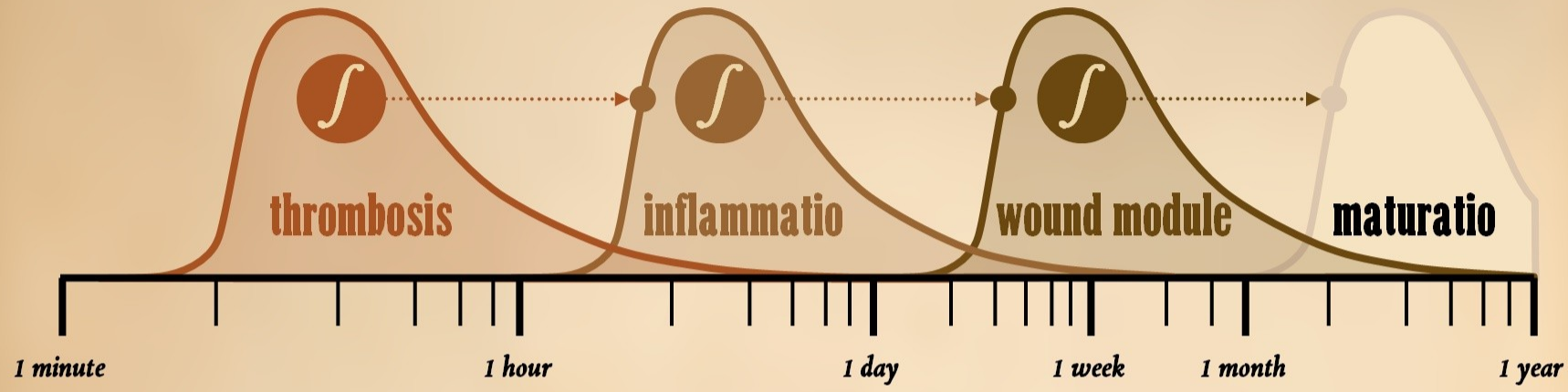
$$d\varphi = v\,\partial r + r\,\partial v$$
$$v = f(\varphi, r)$$
$$r = f(\varphi, v)$$

CARDIAC OUTPUT

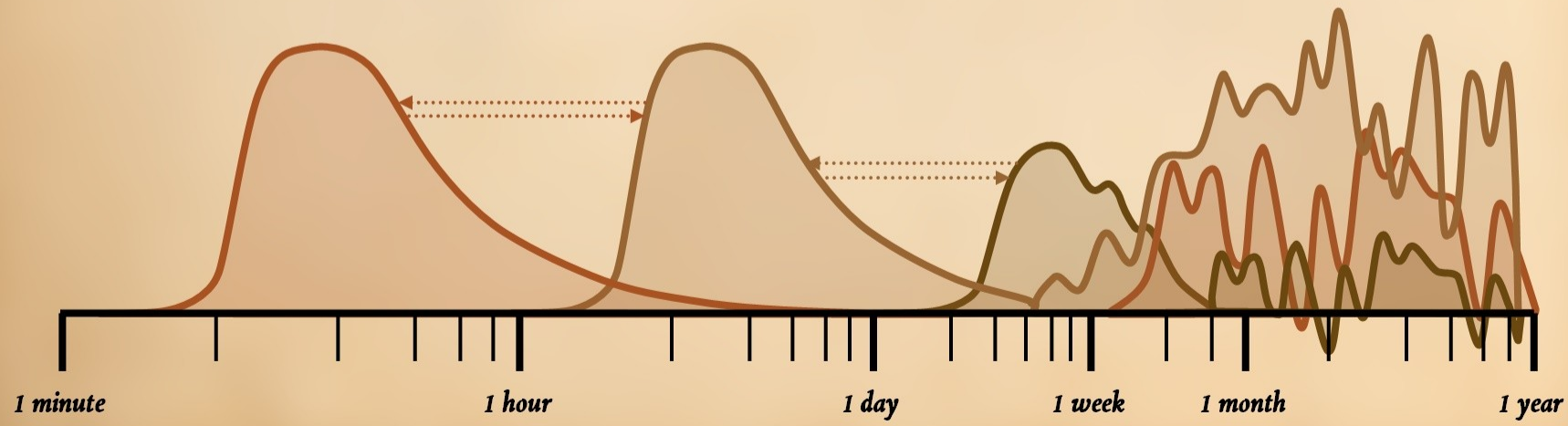
NON-LINEAR DYNAMICS & ITERATION : N-BODY PROBLEMS & MULTI-CONTROL



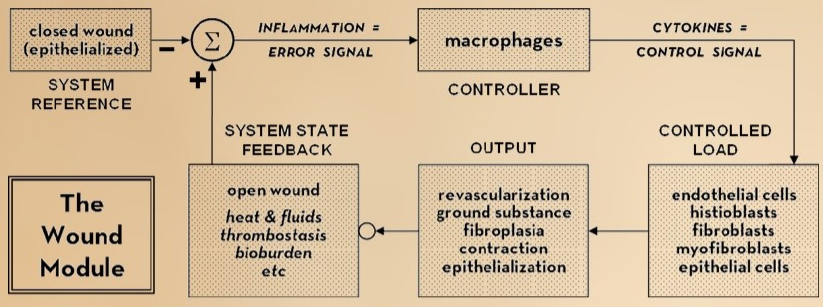
NORMAL HEALTHY RESPONSES = SEQUENTIAL LINEAR ONE-SHOTS

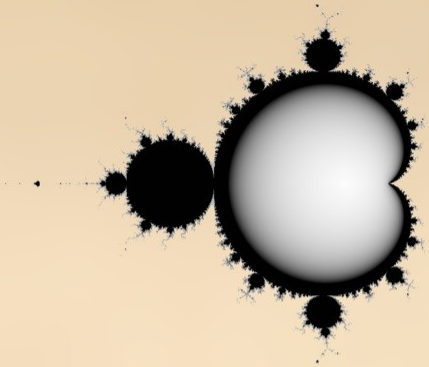


CHRONIC PATHOLOGICAL RESPONSES = NON-LINEAR CHAOS

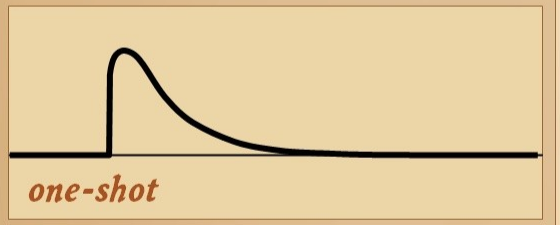


FEEDBACK & CONTROL = NON-LINEARITY = COMPLEX BEHAVIOR & CHAOS :: MORE SO WITH MULTI-CONTROL

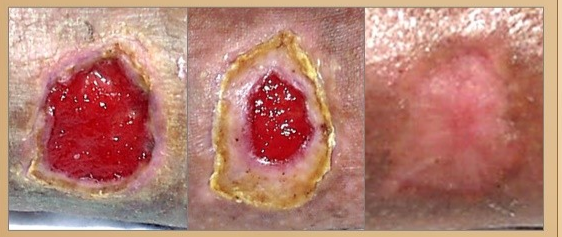




healthy wound - active healing
competent repair - wound module
getting better - closing
convergent

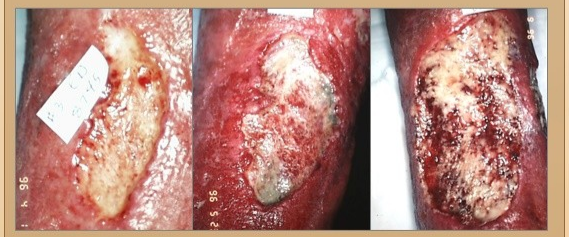


one-shot

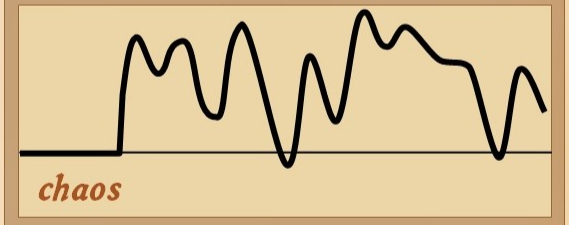


sick wound - active pathology
injury, inflammation, necrosis
getting worse - ulcerating
divergent

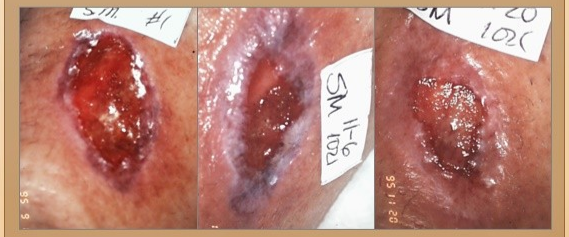
saturation-extinction



impaired wound – orbit dynamics
neither pathological nor improving
mixed, stagnant - no net change
chaotic



chaos



NLD - CHAOS - ATTRACTORS :: CLINICAL IMPLICATIONS

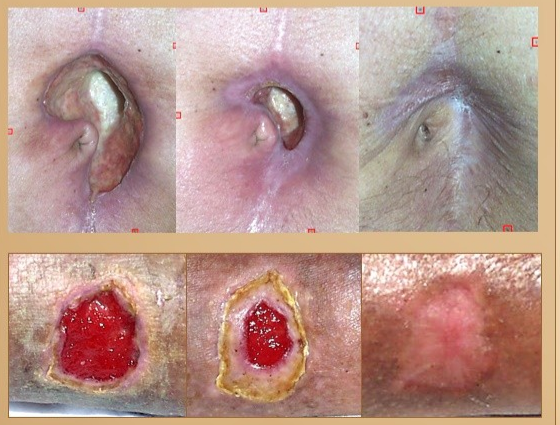
In the problem wound, discriminating active pathology from chaotic behavior is crucial to select proper treatment.

Divergent behavior, i.e. active ulceration, due to active disease & inflammation, must be controlled first before the wound can heal.

When disease, inflammation, & active ulceration are controlled, when the wound exhibits wound module elements but makes no progress, this is chaotic behavior.

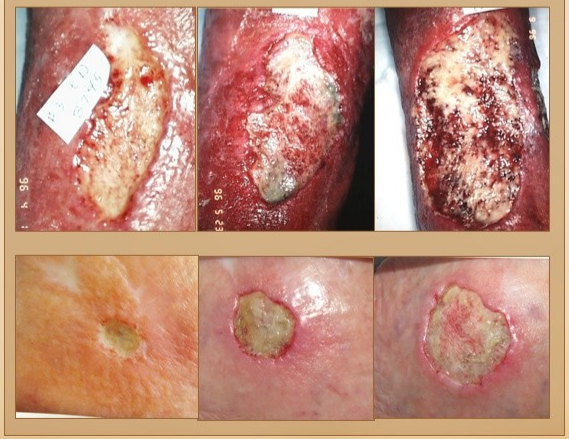
healthy wound - active healing
competent repair - wound module
getting better - closing
convergent

STAY THE COURSE
PREVENT RELAPSE



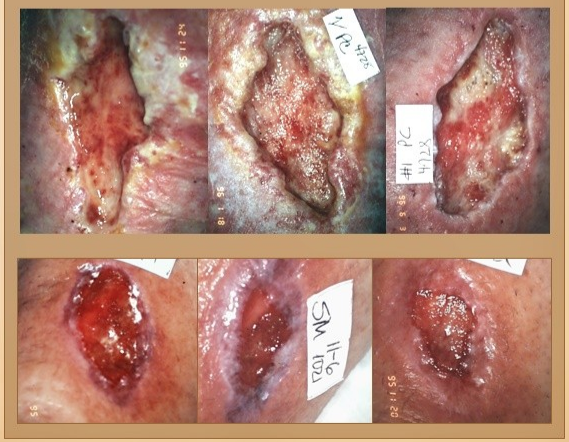
sick wound - active pathology
injury, inflammation, necrosis
getting worse - ulcerating
divergent

TREAT DISEASE
ABORT PATHOLOGY



impaired wound – orbit dynamics
neither pathological nor improving
mixed, stagnant - no net change
chaotic

DISCRETIONARY TREATMENT
TECHNOLOGICAL THERAPIES



NON-LINEAR DYNAMICS & ITERATION

THERMODYNAMICS OF CHAOTIC ATTRACTORS

Non-linear & chaotic systems can have stable attractors . . .
The system tends to dwell or return there.
These basins of attraction are low energy wells.

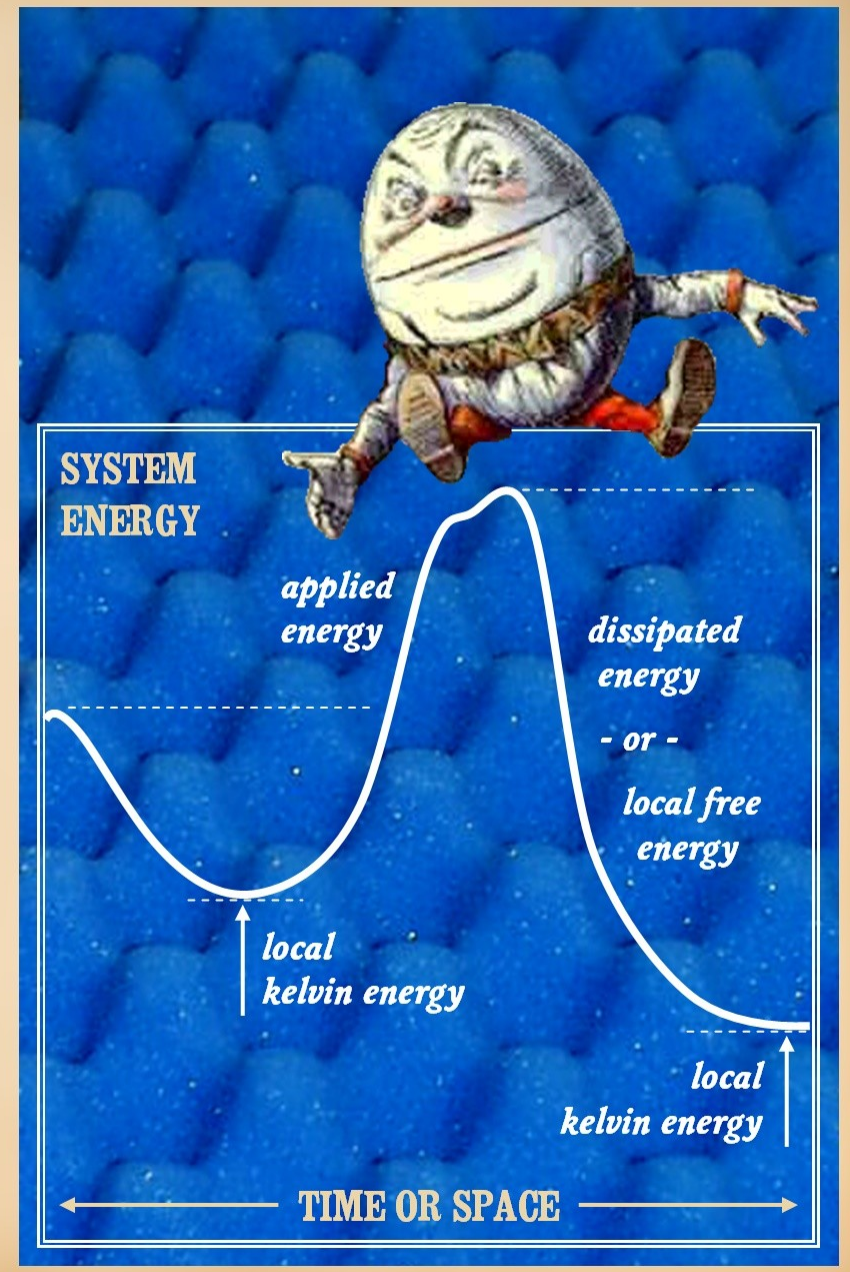
For some, thermodynamics principles apply:
enthalpy
entropy
free energy

Such systems gravitate toward local free energy minima.
Without new energy put in, it can be difficult to displace the system from a low energy attractor.

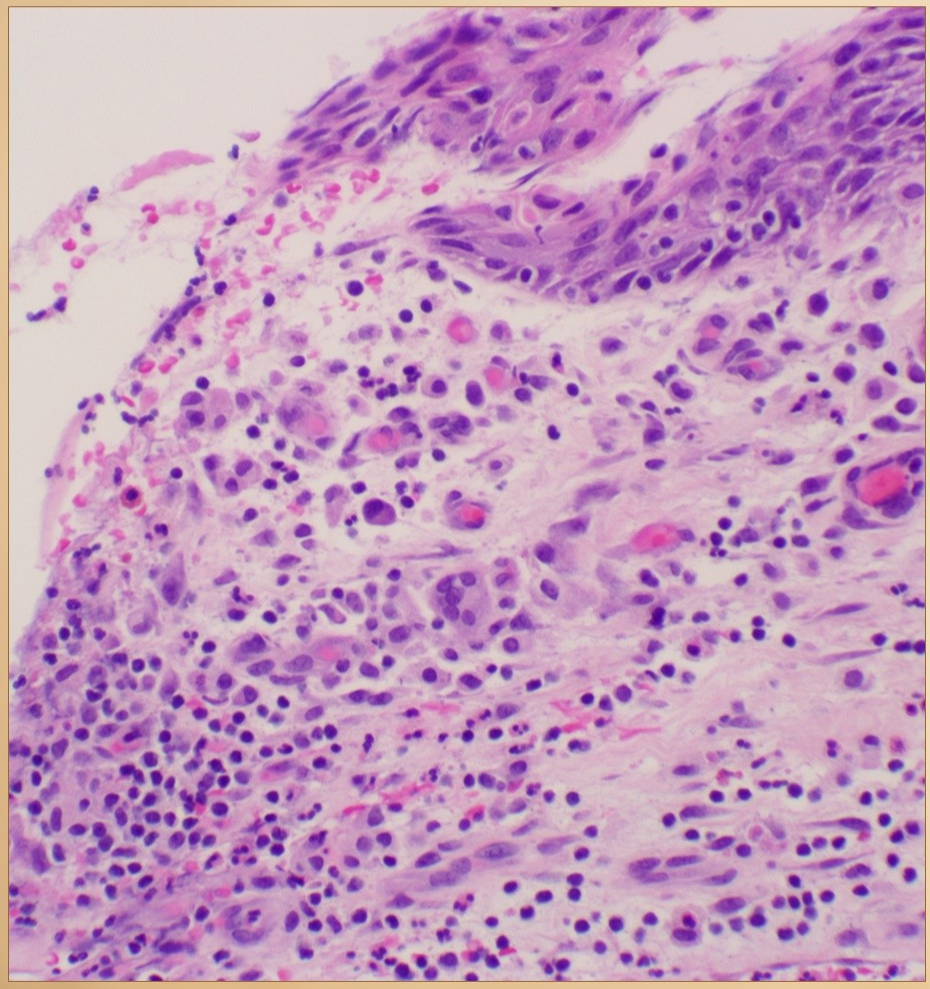
This is why it can be so hard to make CAP wounds heal:
You are trying to break a stable attractor of a chaotic orbit.

They are in a state of effective equilibrium or steady state where free energy is minimized.

Their clinical status may be undesirable, but the chronic persistent chaotic wound is a state of thermo-dynamic stability for that system - it likes being there.



Why does the CAP wound get into a state of dynamical stability, even one that is counter-productive to health ?



CHRONICITY AND THE PATHOLOGY OF WOUND FAILURE

THE RELEVANT PHYSICS OF IMPAIRED WOUND HEALING

NON-LINEAR DYNAMICS

Control

Chaos
Attractors
N-Body Dynamics

Population Logistics

Cellular Automata
& Self-Organization

INTEGRATED WOUND PHYSICS

NON-LINEAR DYNAMICS & POPULATIONS

THE BEHAVIOR OF NON-COMPETITIVE RESOURCE-LIMITED POPULATIONS

P = population

K = maximum population capacity

r = maximum population growth rate

define **x = P/K**

$$\frac{dP}{dt} = rP\left(1 - \frac{P}{K}\right)$$

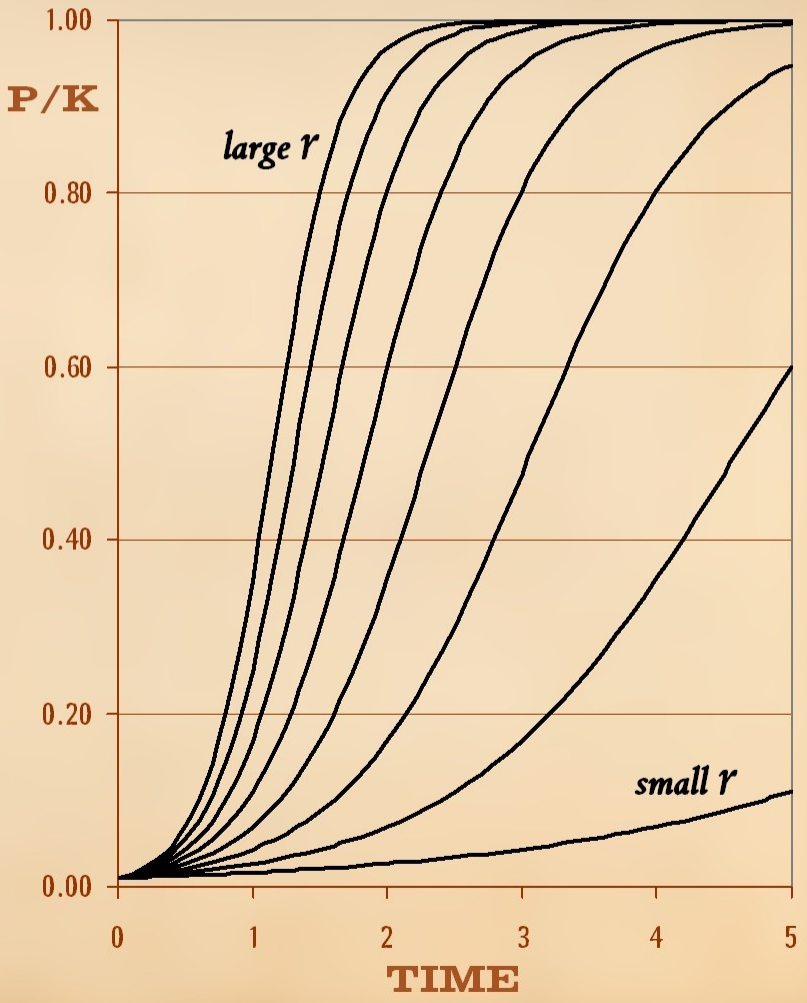
$$\frac{dx}{dt} = rx\left(1 - x\right)$$

$$P(t) = x_0 \frac{K P_0 e^{rt}}{K + P_0\left(e^{rt} - 1\right)}$$

$$x(t) = \frac{x_0}{x_0 + \left(1 - x_0\right) e^{-rt}}$$

THE VERHULST EQUATION

AKA - THE LOGISTICS EQUATION



NON-LINEAR DYNAMICS & POPULATIONS

THE BEHAVIOR OF COMPETITIVE FIXED-RESOURCE POPULATIONS

$$x \leftarrow Ax(1-x)$$

1.50	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50
.375	.438	.500	.563	.625	.688	.750	.813	.875
.352	.431	.500	.554	.586	.591	.563	.495	.383
.342	.429	.500	.556	.607	.665	.738	.812	.827
.338	.429	.500	.555	.597	.613	.580	.495	.501
.335	.429	.500	.556	.602	.653	.731	.812	.875
.334	.429	.500	.556	.599	.624	.590	.495	.383
.334	.429	.500	.556	.600	.646	.726	.812	.827
.334	.429	.500	.556	.600	.629	.597	.495	.501
.333	.429	.500	.556	.600	.642	.722	.812	.875
.333	.429	.500	.556	.600	.632	.603	.495	.383
.333	.429	.500	.556	.600	.639	.718	.812	.827
.333	.429	.500	.556	.600	.634	.607	.495	.501
.333	.429	.500	.556	.600	.638	.716	.812	.875
.333	.429	.500	.556	.600	.635	.610	.495	.383
.333	.429	.500	.556	.600	.637	.713	.812	.827
.333	.429	.500	.556	.600	.636	.613	.495	.501
.333	.429	.500	.556	.600	.637	.711	.812	.875
.333	.429	.500	.556	.600	.636	.616	.495	.383
.333	.429	.500	.556	.600	.637	.710	.812	.827
.333	.429	.500	.556	.600	.636	.618	.495	.501
.333	.429	.500	.556	.600	.637	.708	.812	.875
.333	.429	.500	.556	.600	.636	.620	.495	.383
.333	.429	.500	.556	.600	.636	.707	.812	.827
.333	.429	.500	.556	.600	.636	.622	.495	.501
.333	.429	.500	.556	.600	.636	.706	.812	.875
.333	.429	.500	.556	.600	.636	.623	.495	.383
.333	.429	.500	.556	.600	.636	.704	.812	.827
.333	.429	.500	.556	.600	.636	.625	.495	.501
.333	.429	.500	.556	.600	.636	.703	.812	.875
.333	.429	.500	.556	.600	.636	.626	.495	.383
.333	.429	.500	.556	.600	.636	.703	.812	.827
.333	.429	.500	.556	.600	.636	.627	.495	.501
.333	.429	.500	.556	.600	.636	.702	.812	.875
.333	.429	.500	.556	.600	.636	.628	.495	.383
.333	.429	.500	.556	.600	.636	.701	.812	.827

This function will do 1 of 4 things:

converge to zero

diverge to infinity

enter N-period orbit

never settle – chaos

Values of x vary in complex ways that reflect population dynamics:

predation

deprivation (starvation)

cultivation

sustentation (nutrition)

LOGISTIC DIFFERENCE EQUATION

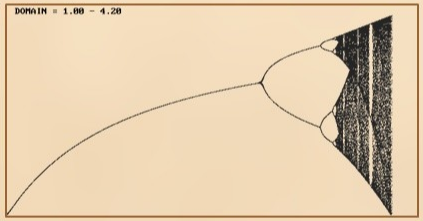
AKA - NON-LINEAR VERHULST

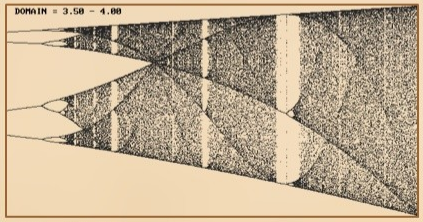
Closed system
Fixed biomass

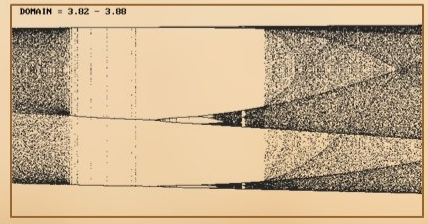
Let :

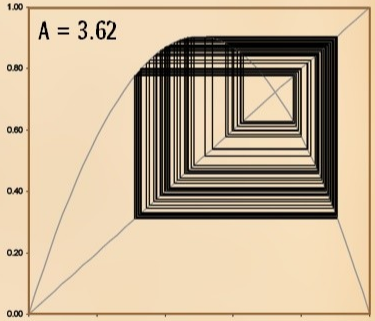
1 = biomass
x = sheep
1 - x = grass

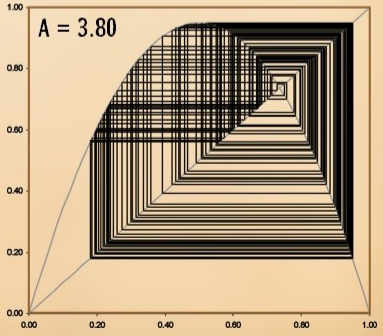
A = growth rate



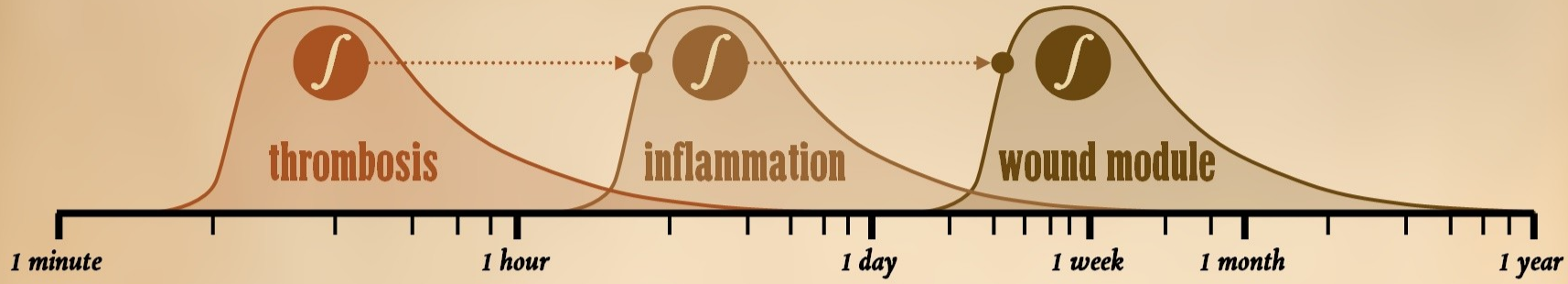


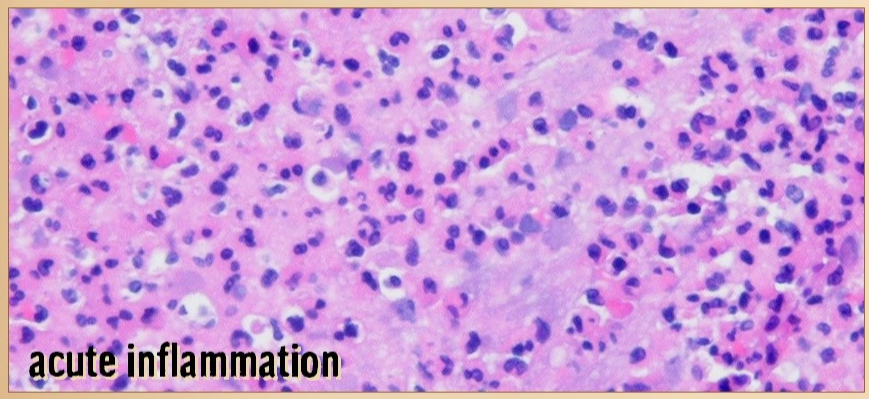


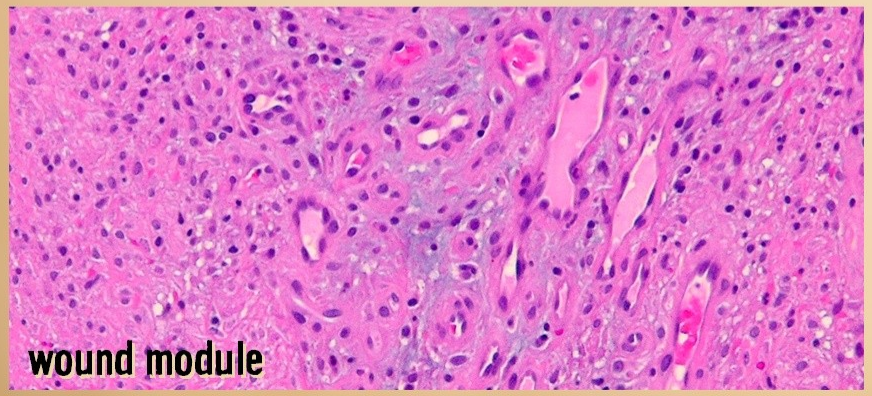


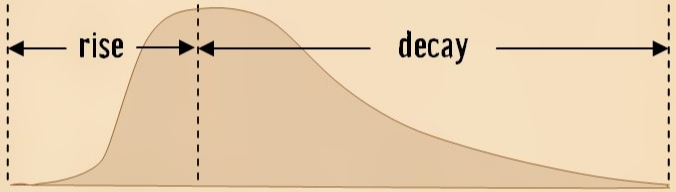


POPULATION LOGISTICS & THE WOUND - HEALTHY & PHYSIOLOGIC









linear Verhulst dynamics

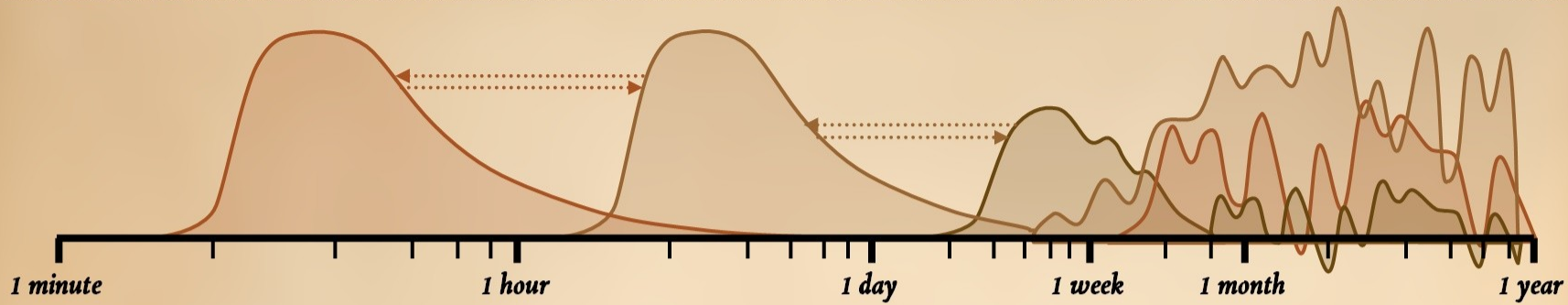
Healthy physiologic wound healing is initiated by injury & thrombosis, then conducted by two cell populations - acute inflammation & wound module.

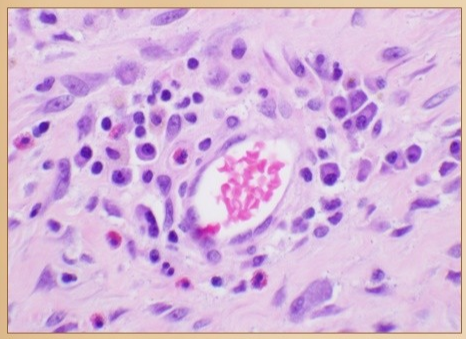
It is a sequence of one-shot self-completing linear events: primary injury & thrombosis -then- acute inflammation -then- wound module.

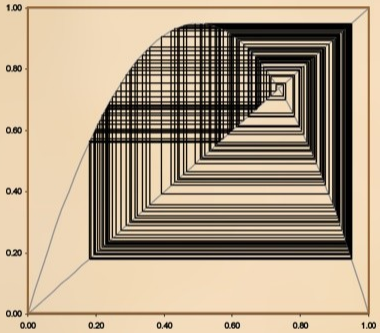
These are non-competitive populations. Each compartment triggers the next but there is no feedback to sustain or re-trigger events.

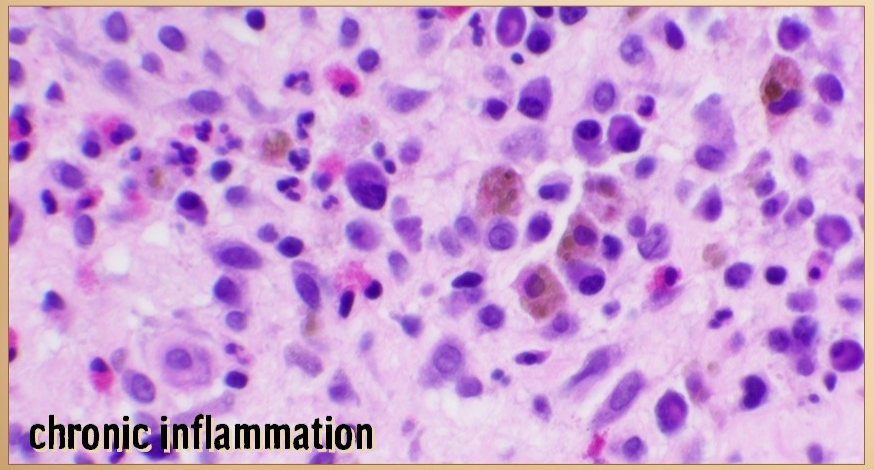
Thus each compartment exhibits Verhulst (sigmoidal) linear dynamics during rise and decay, without complexity, recursion, or instability.

POPULATION LOGISTICS & THE WOUND - IMPAIRED & PATHOLOGIC









Pathologic wound healing occurs when sustained injury, population persistence, non-linear feedback, & abnormal population dependencies sustain compartmental activity.

The two normal cell populations - *acute inflammation* & *wound module* - can develop non-linearity, persistence, & chronicity due to sustained primary injury or thrombosis.

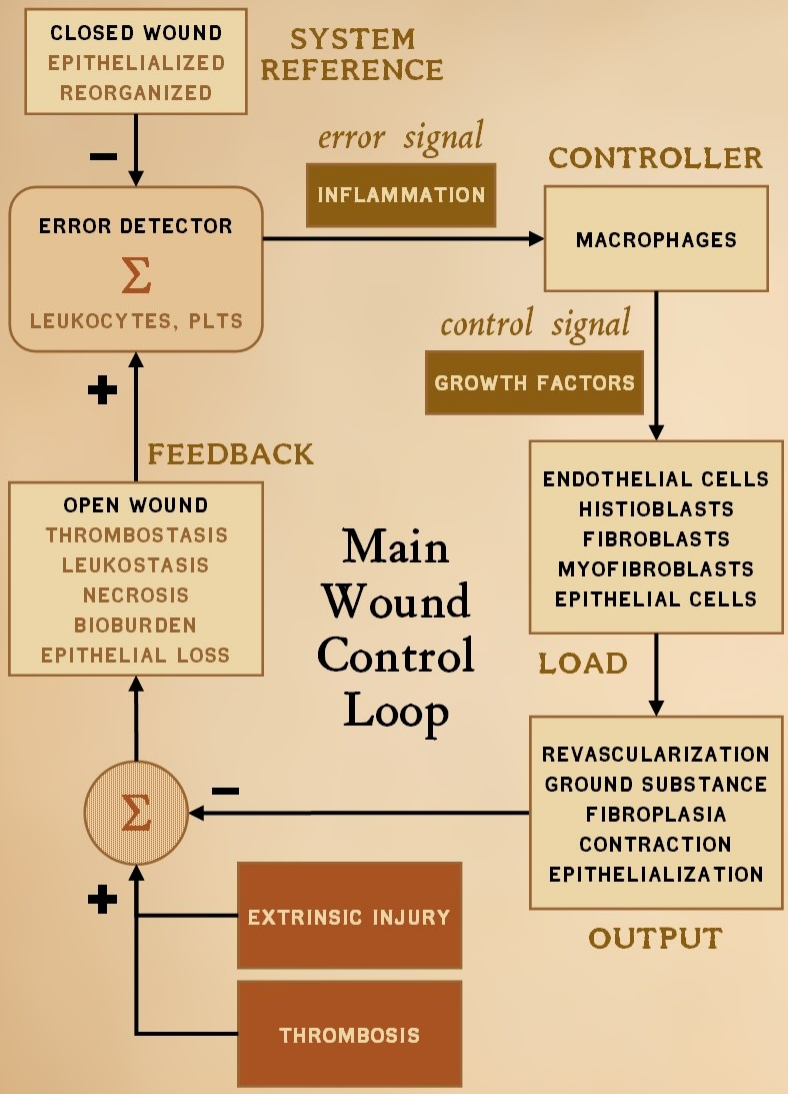
This worsens when pathology, negative dependencies, & chronicity create a 3rd population - *chronic inflammation* - furthering mutual promotion, inhibition, & competition.

This complex mix of dynamics cannot land or converge, consistent with non-linear logistic-difference periodic-chaotic dynamics rather than linear Verhulst dynamics.

Perpetual complexity arises in the logistics of: injury & thrombosis *-vs-* acute inflammation *-vs-* wound module *-vs-* chronic inflammation *-vs-* injury & thrombosis.

When healthy, recurrent primary injury and thrombosis are needed to perpetuate the wound control loop.

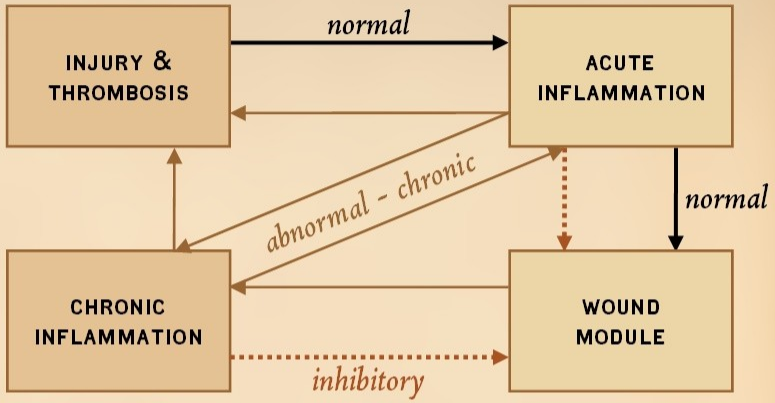
When intrinsic chronicity occurs, the system is locked into a persistent attractor without needing new inputs.



When healthy, recurrent primary injury & thrombosis are needed to perpetuate the wound control loop.

POPULATION LOGISTICS & THE WOUND

IMPAIRED, PATHOLOGIC, CHRONIC

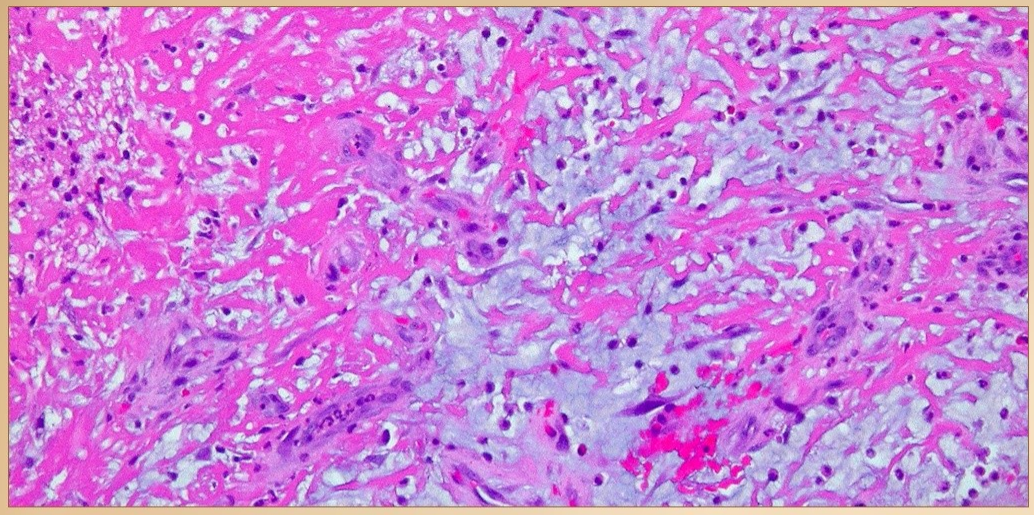


Perpetual complexity arises in the logistics of:
injury & thrombosis *-vs-* acute inflammation
-vs- wound module *-vs-* chronic inflammation
-vs- injury & thrombosis

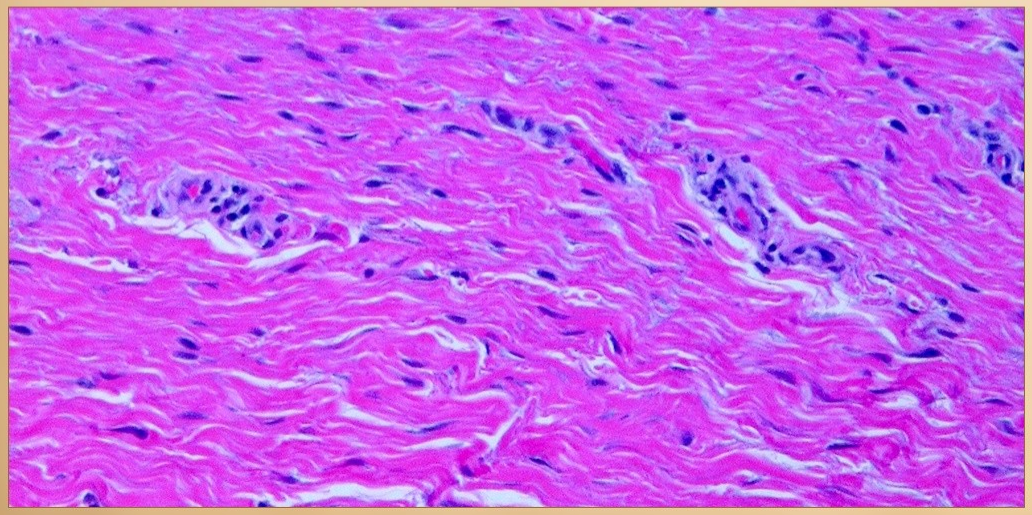
abnormal populations & dependencies =
feedbacks, multicontrol, n-body dynamics
loss of sigmoidal one-shot behavior
chaos & non-converging attractors

stable attractor = low energy well

When intrinsic chronicity occurs, the system is locked into a persistent attractor without needing new inputs.



The Main Control Loop drives wound healing toward the system reference. How does it know what the reference is? How do wound module elements know to organize into the required form that satisfies the reference ?



CHRONICITY AND THE PATHOLOGY OF WOUND FAILURE

THE RELEVANT PHYSICS OF IMPAIRED WOUND HEALING

NON-LINEAR DYNAMICS

Control

Chaos
Attractors
N-Body Dynamics

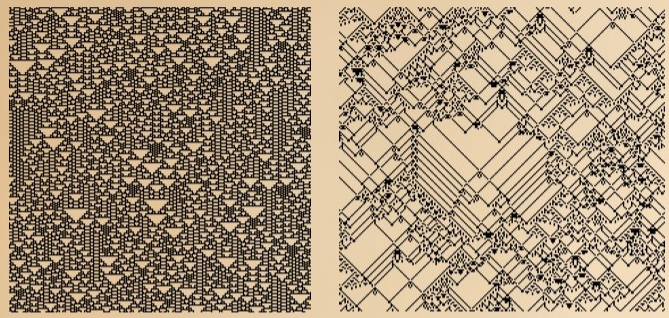
Population Logistics

Cellular Automata
& Self-Organization

INTEGRATED WOUND PHYSICS

CELLULAR AUTOMATA

SELF-ORGANIZATION



MATRIX AUTOMATA

DLA – DIFFUSION LIMITED AGGREGATION

CELLULAR AUTOMATA

Self-organizing automata are a
foundational concept in non-linear dynamics.

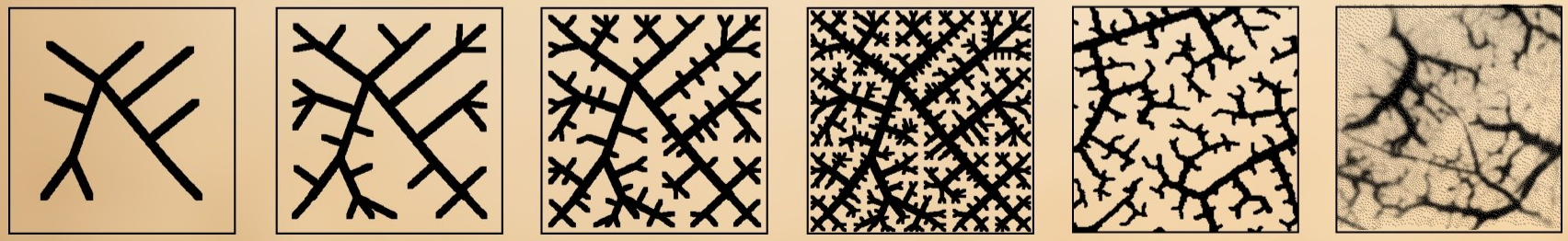
They are systems in which individual elements, "cells", have a set of strict deterministic rules governing their behavior and how they must interact and evolve with adjacent or local cells.

If you throw them all into a pot, they will sort themselves out, generally ending up with complex highly organized structures based on just a few simple instructions or relationships.

PARSIMONIOUS SELF-ORGANIZATION

The route to self–assembly that takes
the least information or energy or effort.

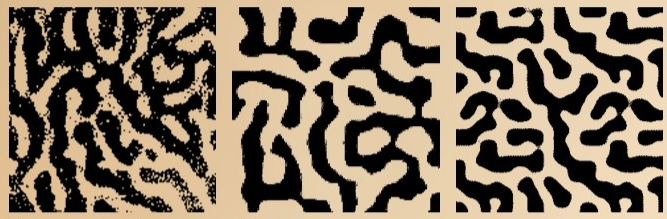
This is how natural systems behave.
There is a thermodynamic basis for this,
optimizing changes in free energy and entropy.



VT – VASCULAR NET ANGIOGENESIS

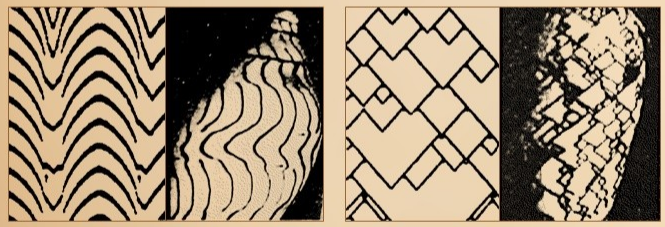
CELLULAR AUTOMATA

BIOLOGICAL SYSTEMS



OCULAR DOMINANCE COLUMNS

ANIMAL COATS



MOLLUSC PATTERNS

Biological structures are all assembled by cellular automata exhibiting parsimonious self-organization.

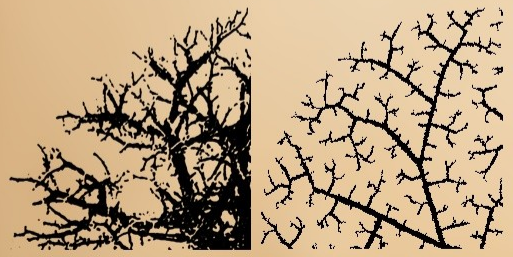
There are no morphology genes, just structural proteins and process proteins. It is in their inter-operations that complex organization and macro-structure occurs.

The self-assembly of tissues and organs occurs due to limited sets of "instructions", operating by deterministic physics, which govern how cells interact with local neighbors.

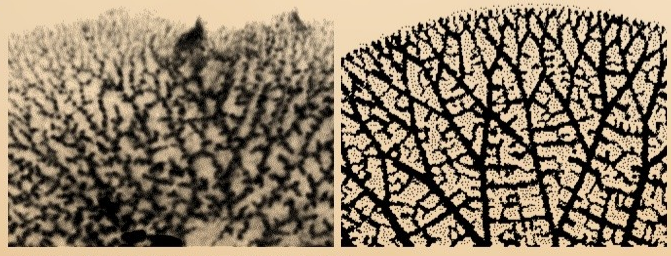
Non-linearity, feedback, and control are implicit & explicit.

Wound repair & the wound module are just another example of this kind of automatic self-assembly and parsimonious self-organization / self-re-organization.

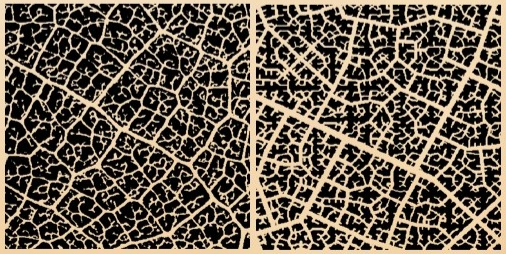
When allowed to function properly, stromal rebuilding is automatic and correct, without any blueprint or collective knowledge by the cells of what is being built.



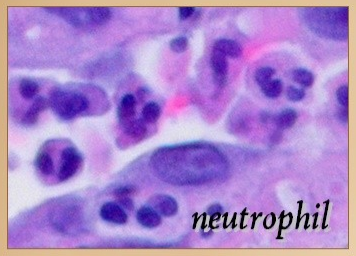
BILE DUCTS

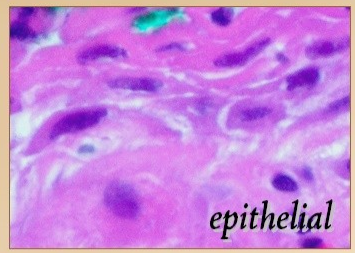


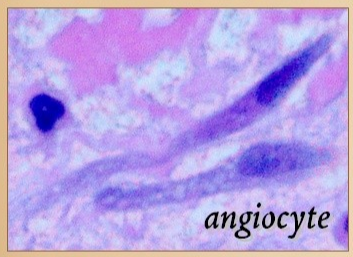
GASTROVASCULAR SYSTEMS

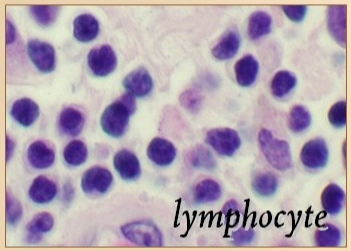


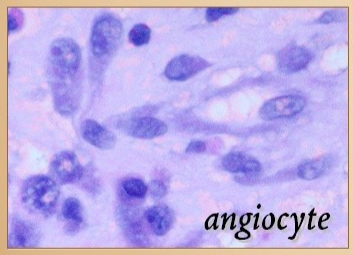
LEAF VEINS

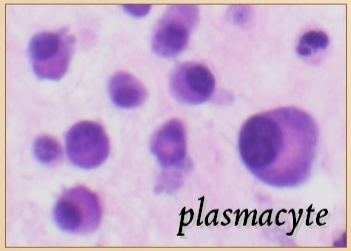


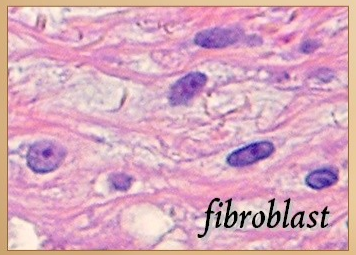


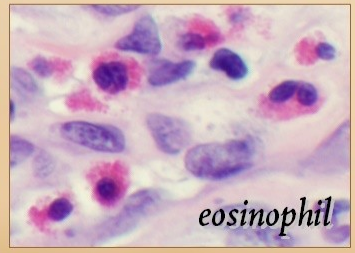












CELLULAR AUTOMATA

Wound Self-Assembly & Stromal Reorganization

The wound is a cellular self-organizing automatic system.
It is made of real biological cells. Their deterministic interactions are epitomized in the Main Control Loop.

Each cell - monocyte, angiocyte, fibroblast, keratinocyte –
has an assigned job. If allowed to function properly, stromal rebuilding & wound closure are automatic and correct.

When pathological, self-organization is disturbed or fails.
Wound healing is then disrupted - because wound healing is nothing more than the self-organization of these cells.

Problems happen when chronic inflammatory cells appear.
They disturb the function & organization of the cells meant to be there, arresting or disrupting their intended organization.

In the chronic chaotic intrinsically pathological wound,
NOT ONE OF THESE CELLS IS INTRINSICALLY PATHOLOGICAL.

Each cell and cell type is intrinsically correct or healthy, trying to do what it is meant to do. If it is failing, it is because it is being besieged, restrained, or deprived by another of these cells.

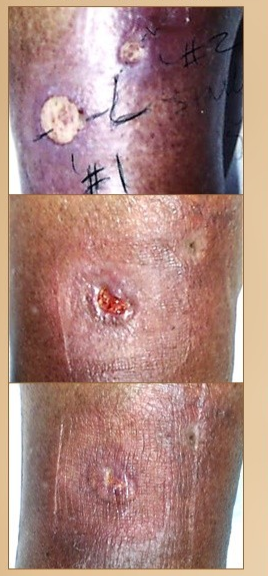
Are there intrinsic disorders of the repair cells? No. See the website & text.

These are not divergent wounds - they are not ulcerating and getting worse. They are just not healing. What is disrupted is ONLY the aggregate organization and self-assembly.

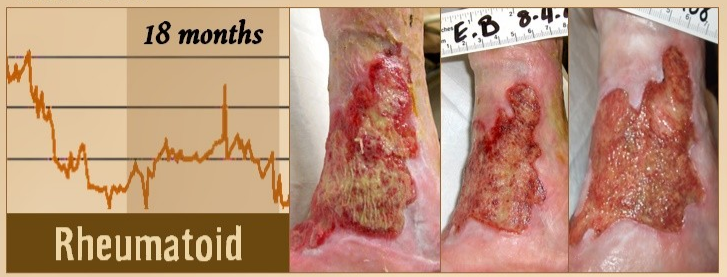
CHRONICITY AND THE PATHOLOGY OF WOUND FAILURE

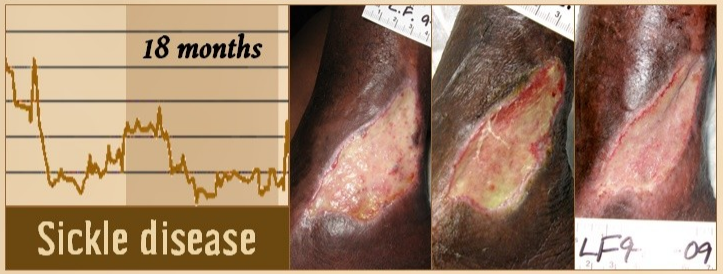
THE RELEVANT PHYSICS OF IMPAIRED WOUND HEALING

CONVERGENT

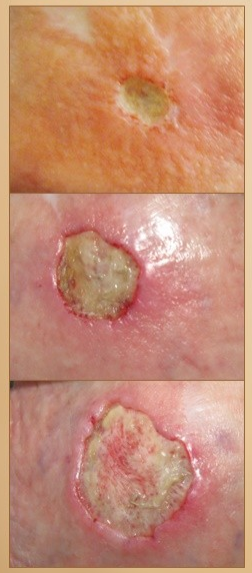


CHAOTIC





DIVERGENT



Some wounds refuse to heal, even when gross pathology & causative disease are controlled and acute ulceration and inflammation are subsided.

THERE IS A REASON

these wounds go back and forth but get no better
they cannot spontaneously climb out of this attractor
multiple therapeutics are often of no benefit
adverse behavior is independent of the primary pathology

THESE REASONS CANNOT BE UNDERSTOOD

by looking at any individual cell or chemical or gene
by analysis of any dependent-vs-independent experiment
by any "conventional bioscience" type of experiment
by any type of randomized controlled trial

NON-LINEAR DYNAMICS

Control

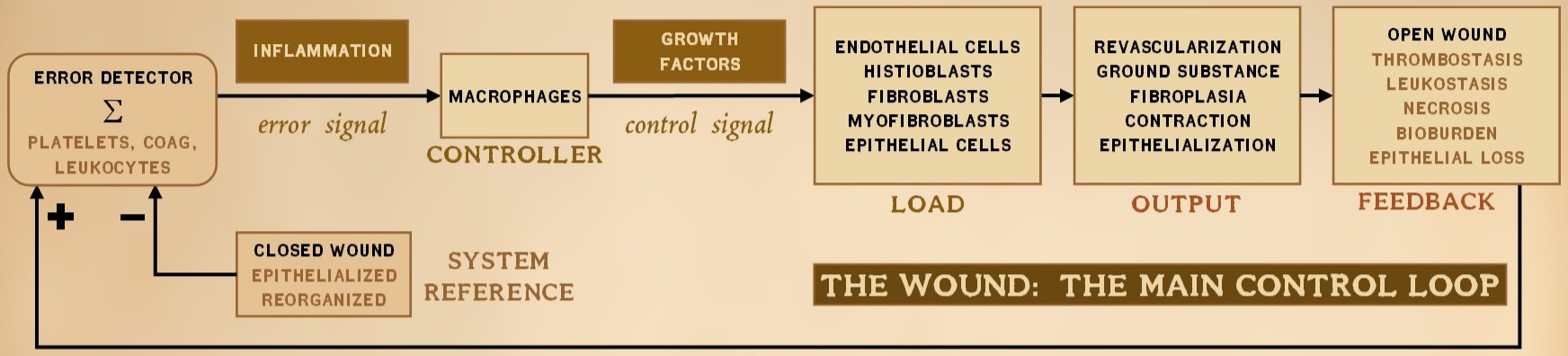
Chaos
Attractors
N-Body Dynamics

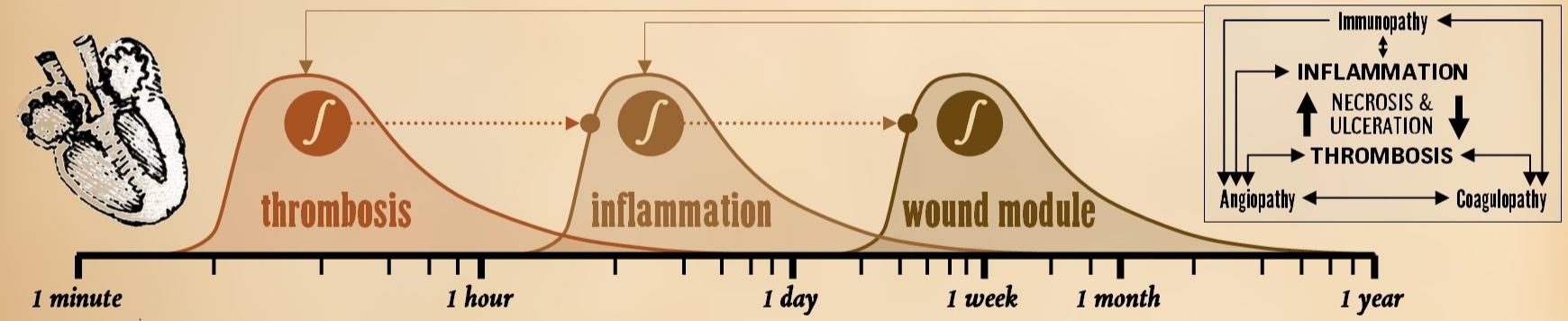
Population Logistics

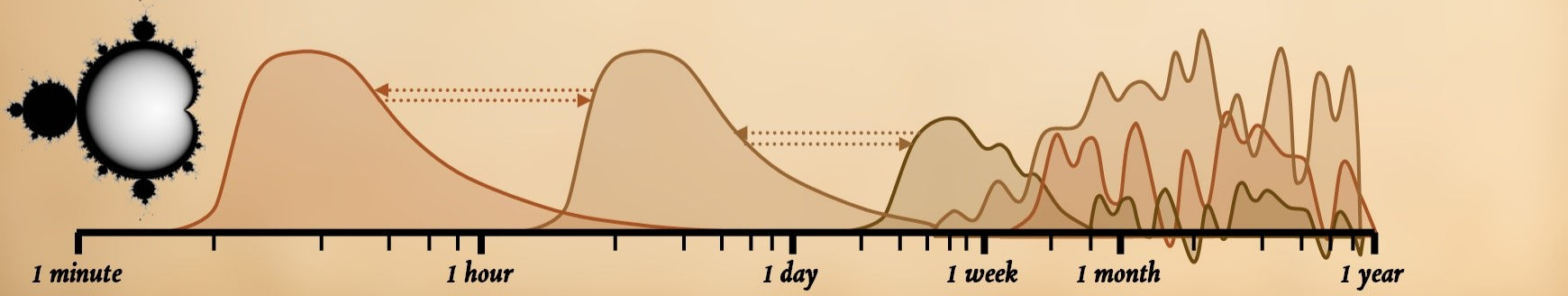
Cellular Automata
& Self-Organization

INTEGRATED WOUND PHYSICS

NON-LINEAR DYNAMICS : FEEDBACK, CONTROL, CHAOS, ATTRACTORS, N-BODY MULTI-CONTROL





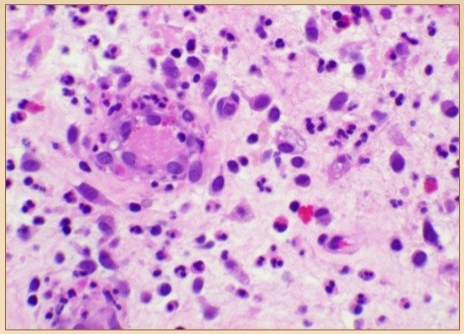


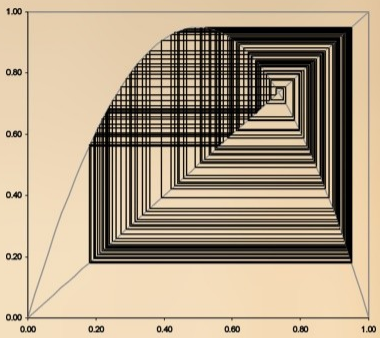
NLD : POPULATION LOGISTICS & DEPENDENCIES, CELLULAR AUTOMATA & SELF-ORGANIZATION

Why does the CAP wound get into a state of unhealed dynamical stability, even one that is counter-productive to health ?

population logistics

abnormal populations
abnormal dependencies

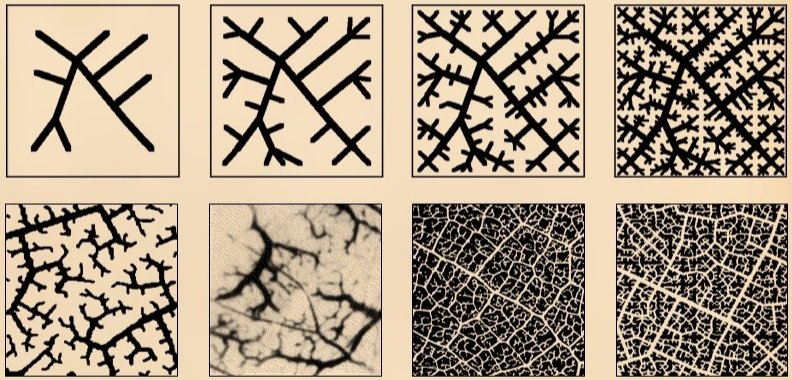




The Main Control Loop drives wound healing toward a reference. What is the reference? How do wound module elements know to organize into the required form that satisfies the reference ?

cellular automata & self-organization

parsimonious self-assembly
thermodynamic stability



In the chronic chaotic intrinsically pathological wound,

NOT ONE OF THE CELLS IS INTRINSICALLY PATHOLOGICAL.

These are not divergent wounds - not ulcerating and getting worse. They just are not healing. What is disrupted is ONLY the aggregate organization and self-assembly.

(The specific chemicals degraded, disorganized, & denied are a matter for conventional biosciences to discover.)

When healthy, recurrent primary injury & thrombosis are needed to perpetuate the wound control loop.

When intrinsic chronicity occurs, the system is locked into a persistent attractor without needing new inputs.

When healthy, recurrent primary injury & thrombosis are needed to perpetuate the wound control loop.

When intrinsic chronicity occurs, the system is locked into a persistent attractor without needing new inputs.

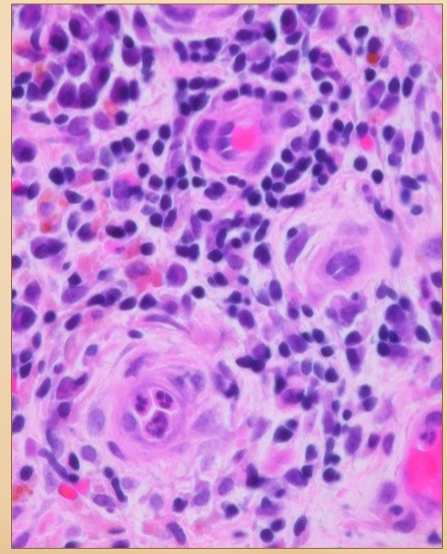
ACUTE WOUNDS	CHRONIC - EXTRINSIC	CHRONIC - INTRINSIC
incidental injury	repetitive primary injury untreated disease uncontrolled wound	sustained primary injury persistent disease uncontrolled wound
↓	↓	↓
sequential one-shots normal healing	2-population chaos - vs - non-chaotic due to disease divergence or delayed convergence	autonomous chaotic attractor auto-immunization 3rd population

Underlying primary inducing disorders: inflammation (reactive & induced), infection-immunity, trauma-injury, allergy-atopy, thrombosis & micro-occlusion

All cells have specific parsimonious biologically defined functions . . . including chronic inflammation cells, the 3rd population of the pathological wound.

CHRONIC INFLAMMATION

! IS NOT !
THE RELIEF TEAM



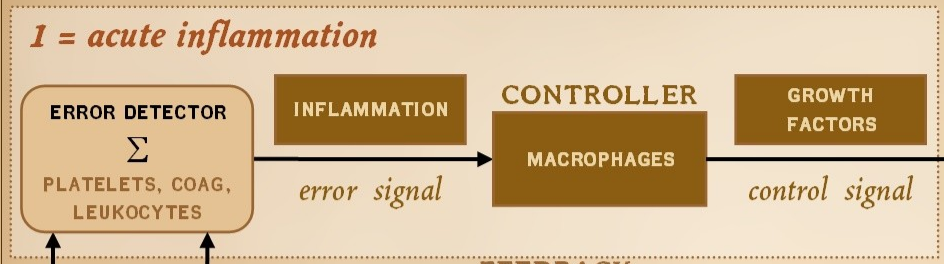
" WOMEN 20-34 YEARS - INFILTRATION OF VESSEL WALL BY MONONUCLEAR CELLS, MAINLY LYMPHOCYTES - 4 PATIENTS ANTIPHOSPHOLIPID ANTIBODIES - ONE HETEROZYGOUS FACTOR V LEIDEN - WE TERM THIS LYMPHOCYTIC THROMBOPHILIC ARTERITIS "

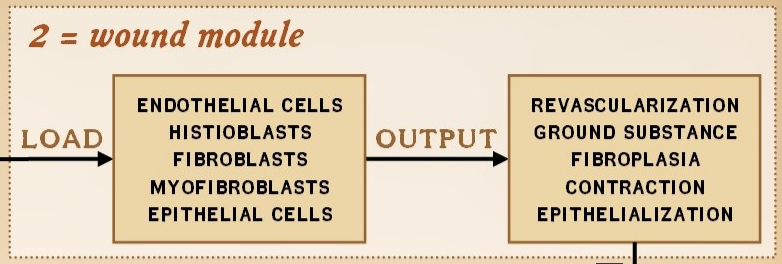
" CRITERIA FOR LYMPHOCYTIC VASCULITIS (1) LYMPHOCYTIC INFILTRATE BLOOD VESSEL, (2) FIBRINOID NECROSIS, (3) ENDOTHELIAL CELL HYPERPLASIA - CLINICAL DIAGNOSES VARIED - DRUG REACTION, CHRONIC URTICARIA, NODULAR SCABIES, ERYTHEMA MULTIFORME, - PROBABLY NOT SPECIFIC - MORE LIKELY A REACTIVE PROCESS "

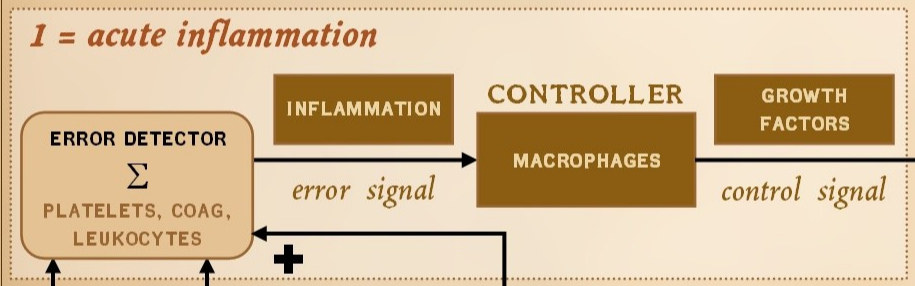
" LYMPHOCYTIC VASCULITIS AS SIGN OF EARLY CONNECTIVE TISSUE DISEASE - HEMORRHAGIC ACRAL LIVEDO WITH ANTI-RIBONUCLEO-PROTEIN ANTIBODIES - STRIKING LYMPHOCYTIC VASCULAR REACTION - , PERIVASCULAR EXTRAVASATION OF RED CELLS, LEUKOCYTOCLASTIC DEBRIS - FINALLY DEVELOPED SYSTEMIC LUPUS ERYTHEMATOSUS "

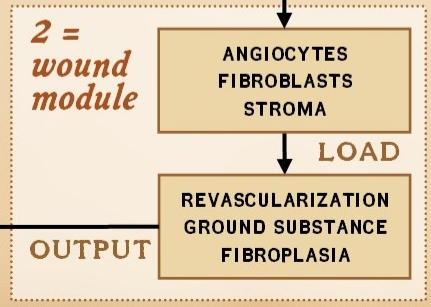
" LYMPHOCYTIC VASCULITIS - CORRELATES WITH BROAD CLINICAL DIFFERENTIAL DIAGNOSIS - CONNECTIVE TISSUE DISEASE (MOSTLY SLE), RICKETTSIA AND VIRUSES, IDIOPATHIC LICHENOID DERMATOSES, PERNIOSIS, ULCERATIVE NECROTIC MUCHA-HABERMANN "

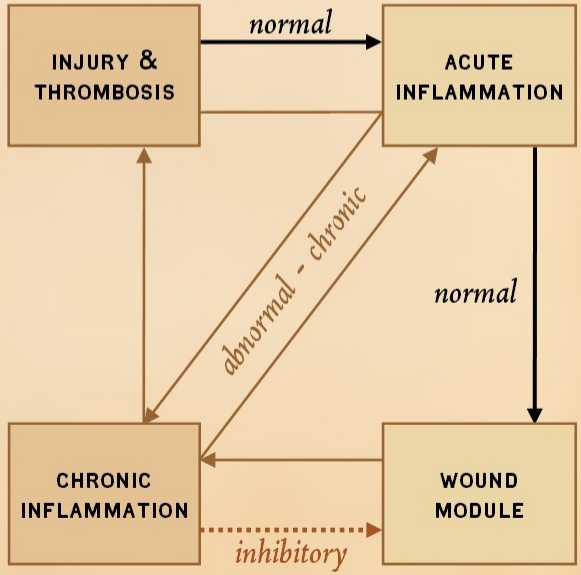
WOUND FAILURE & CHRONICITY : EXTRINSIC 2-BODY VS INTRINSIC 3-BODY



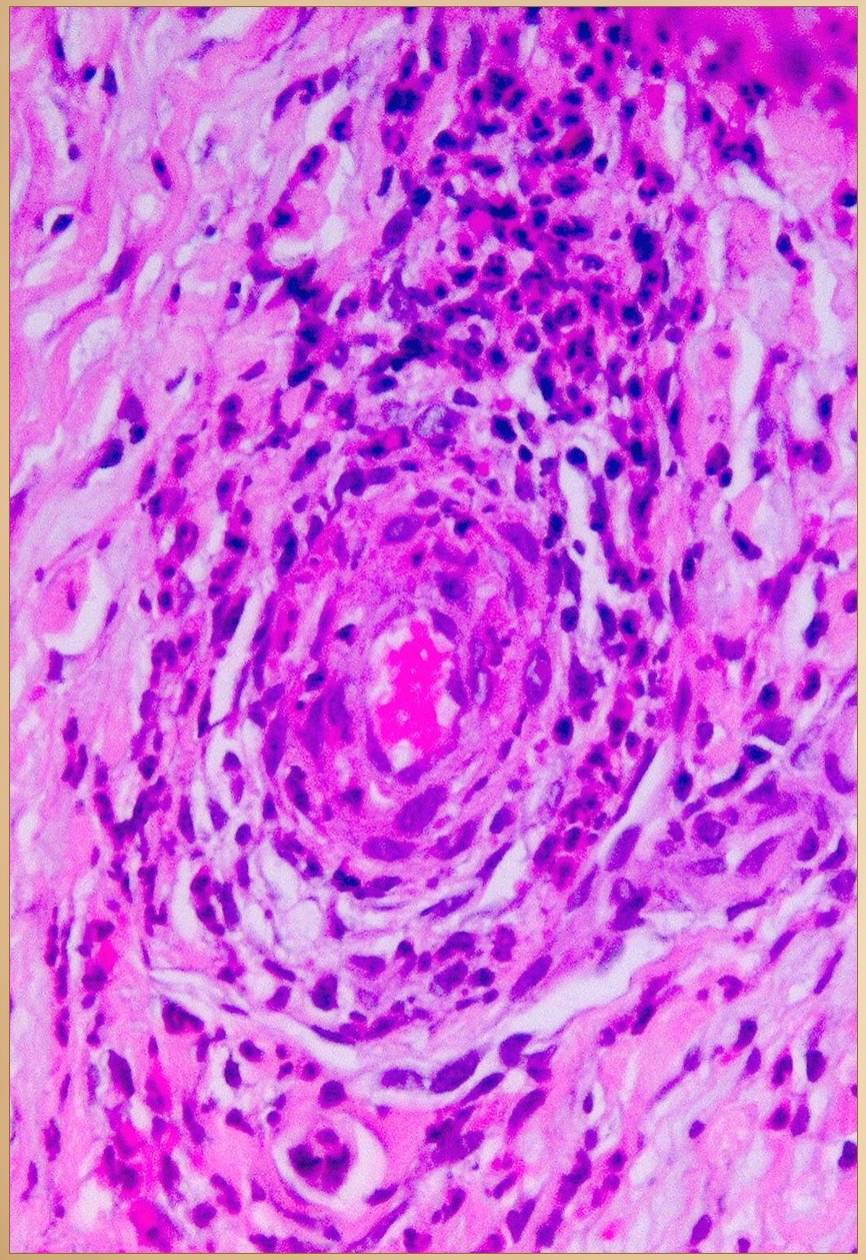


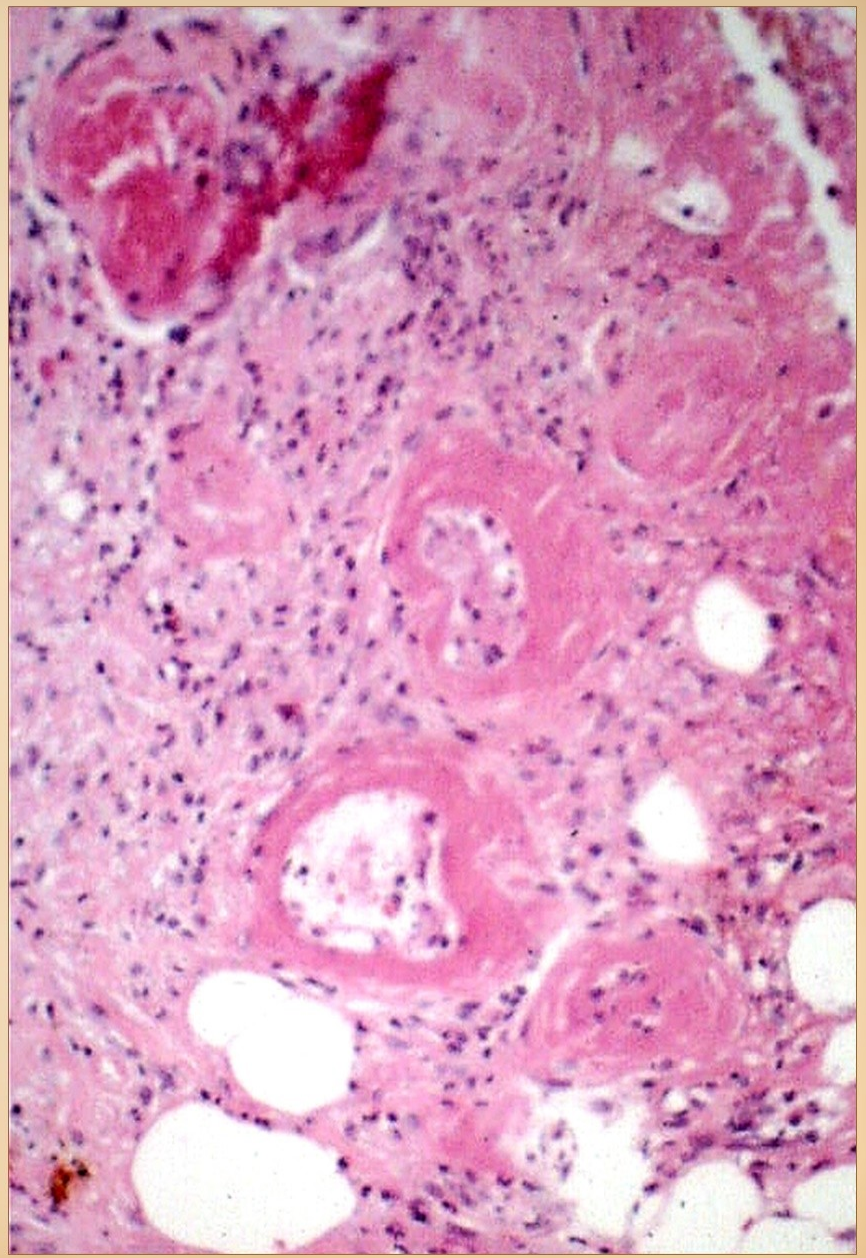






RECURRENT INJURY, INFLAMMATION, AND THROMBOSIS CAN PERPETUATE THE WOUND CONTROL LOOP





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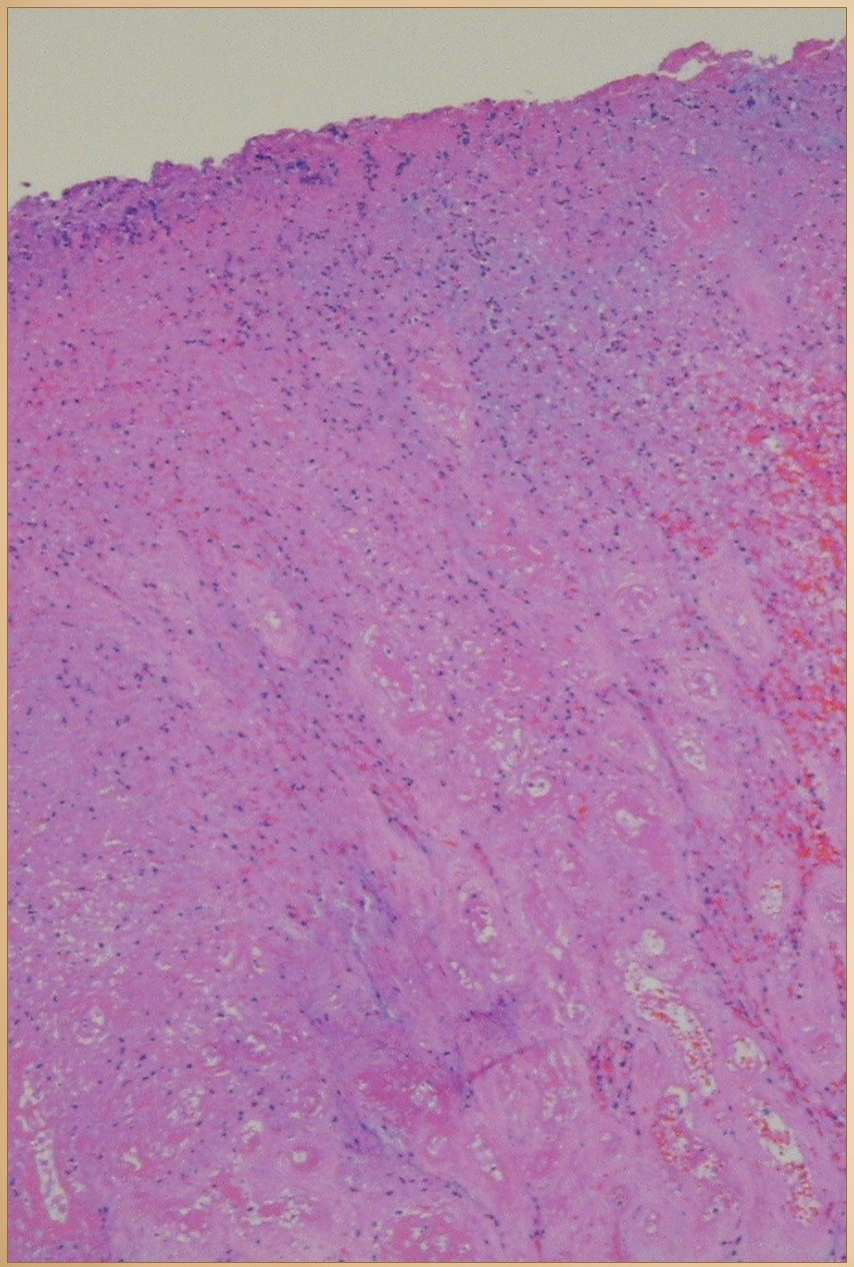
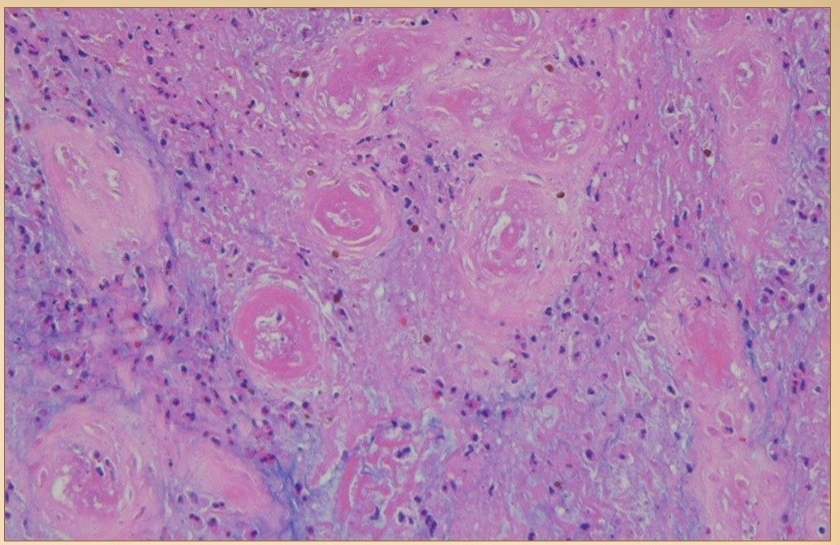
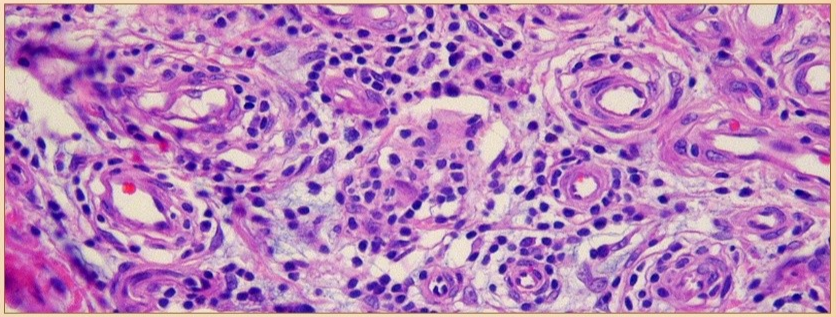
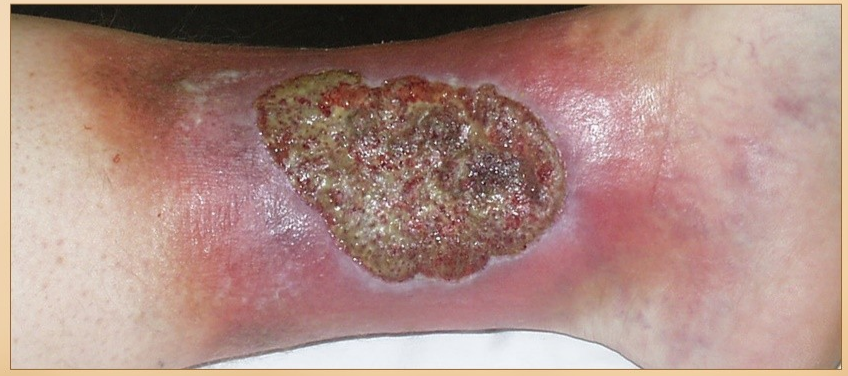
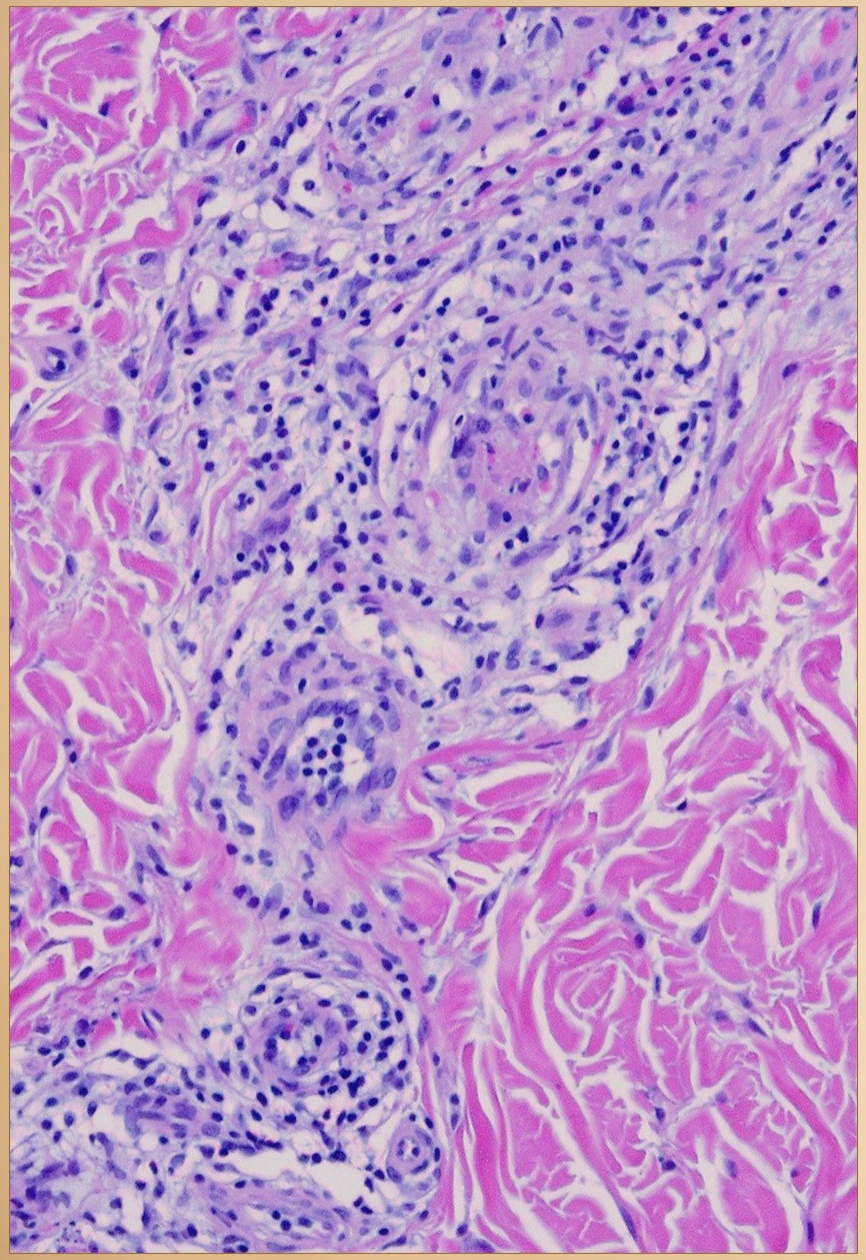


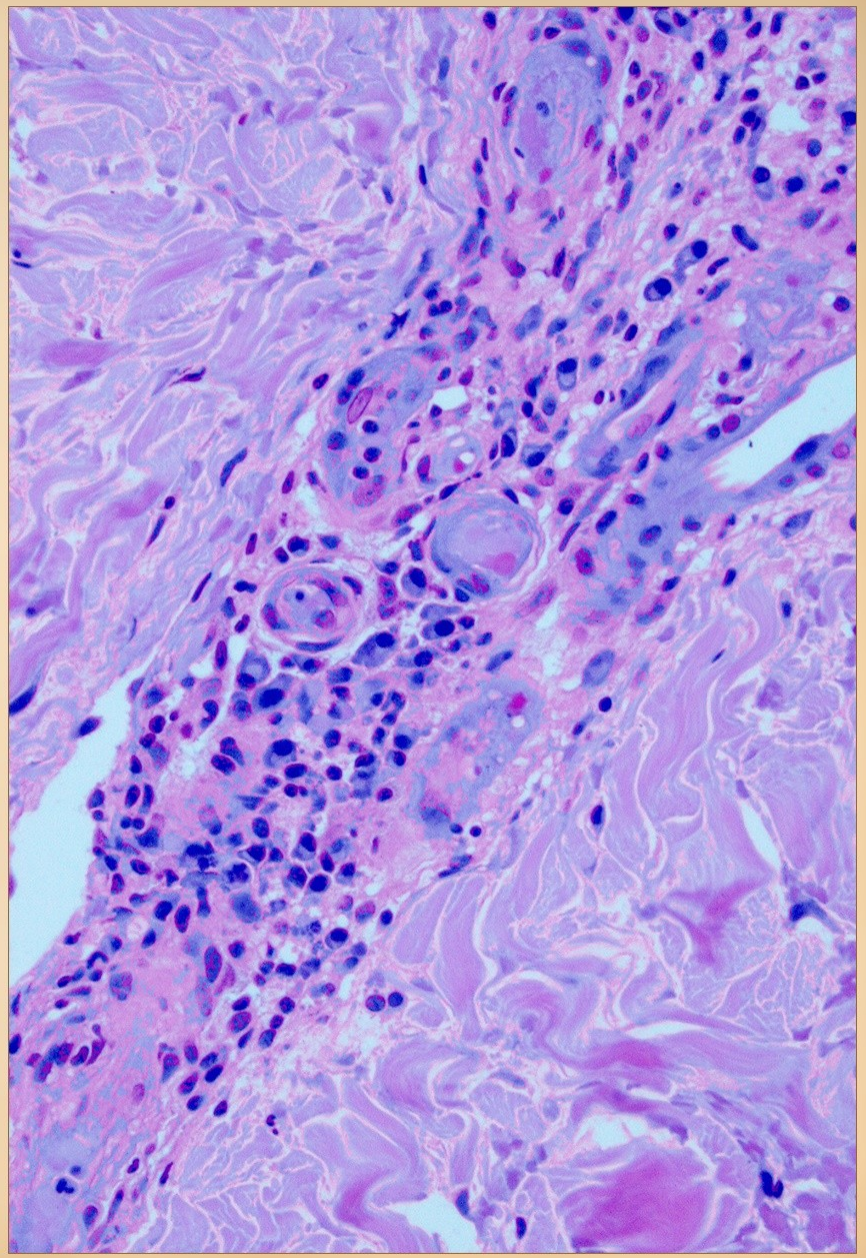






CHRONIC INFLAMMATION = THREE DEPENDENT POPULATIONS = FAILED ORGANIZATION = NON-HEALING





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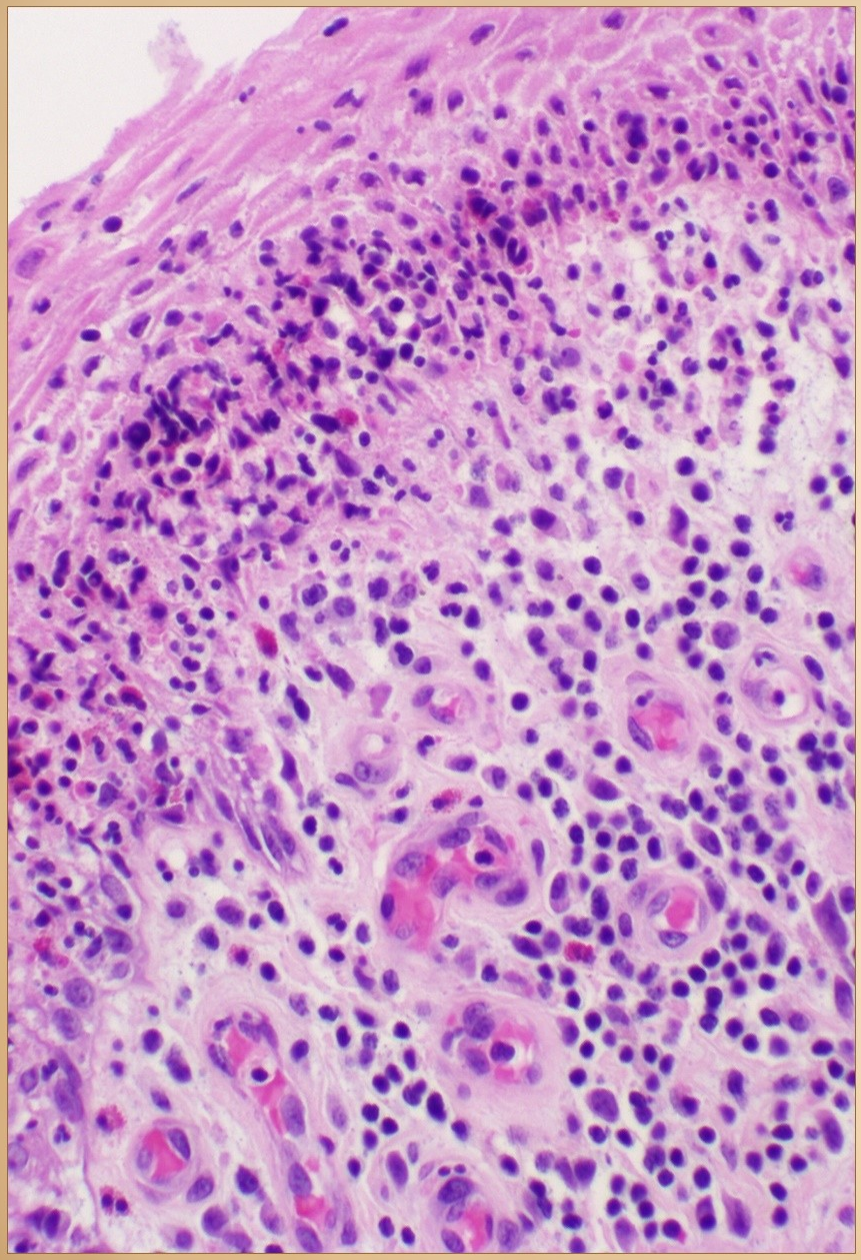

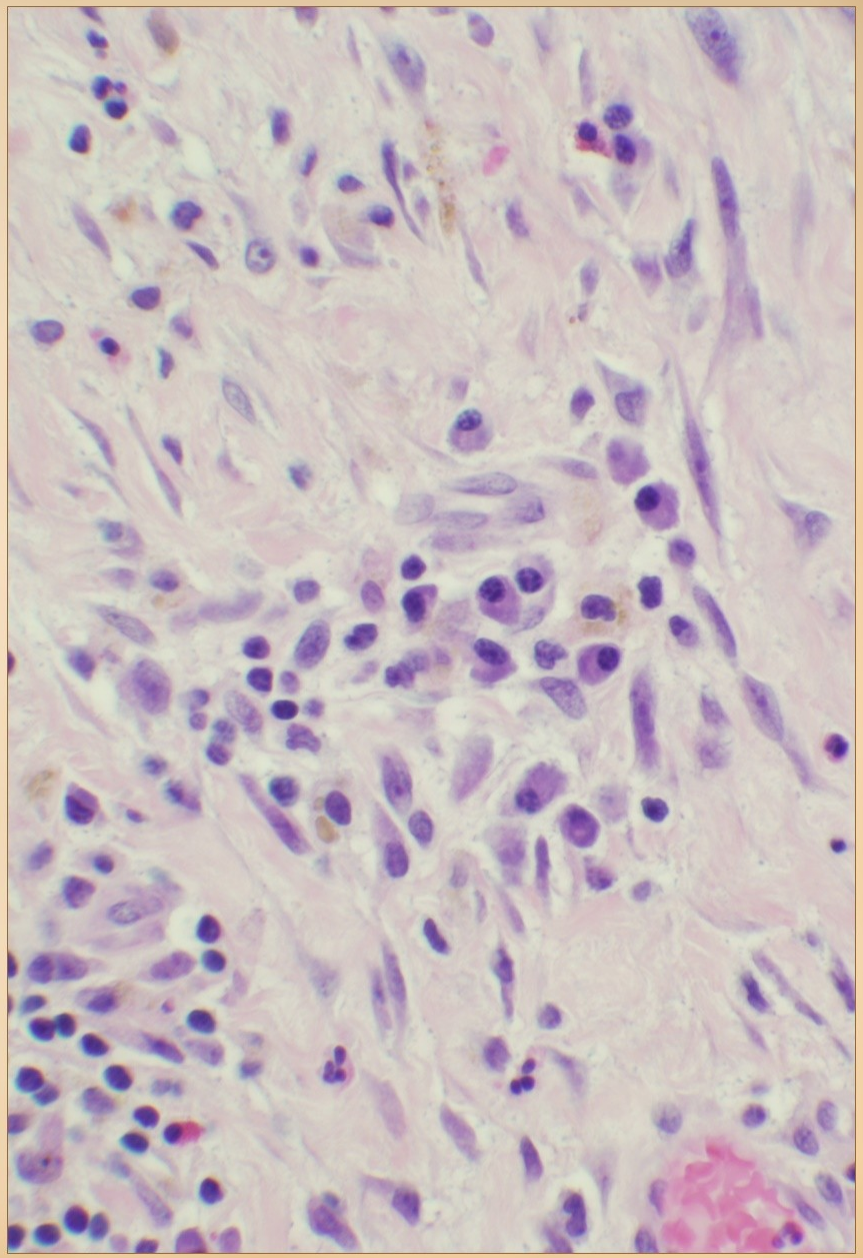

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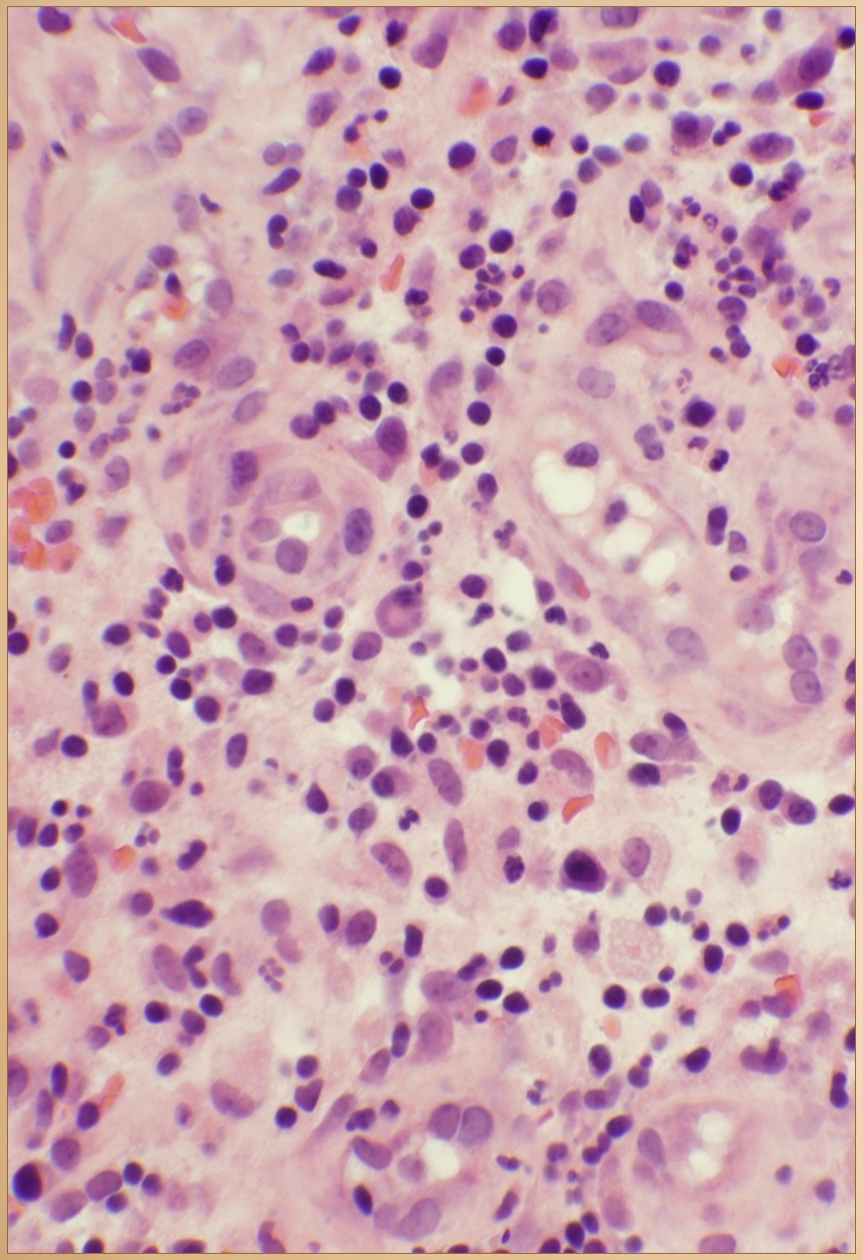

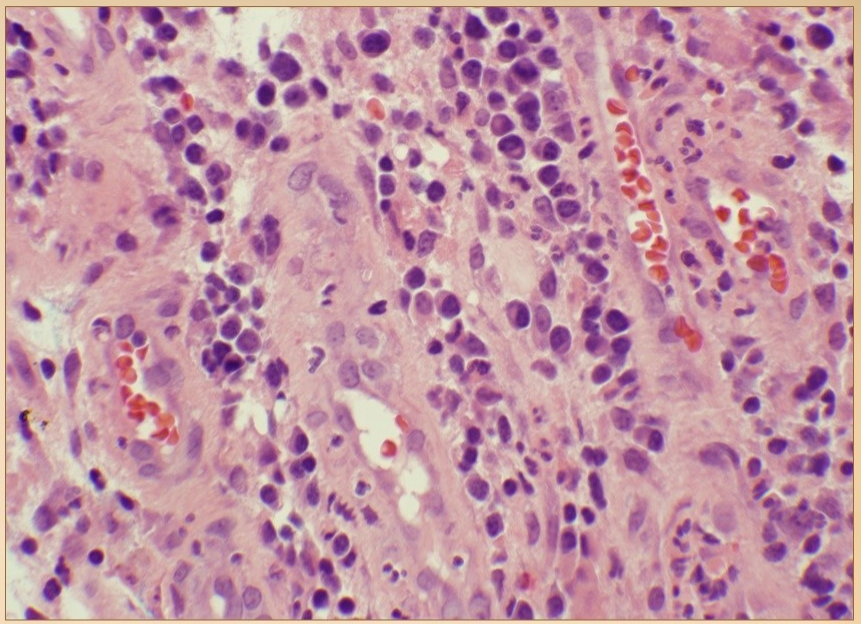

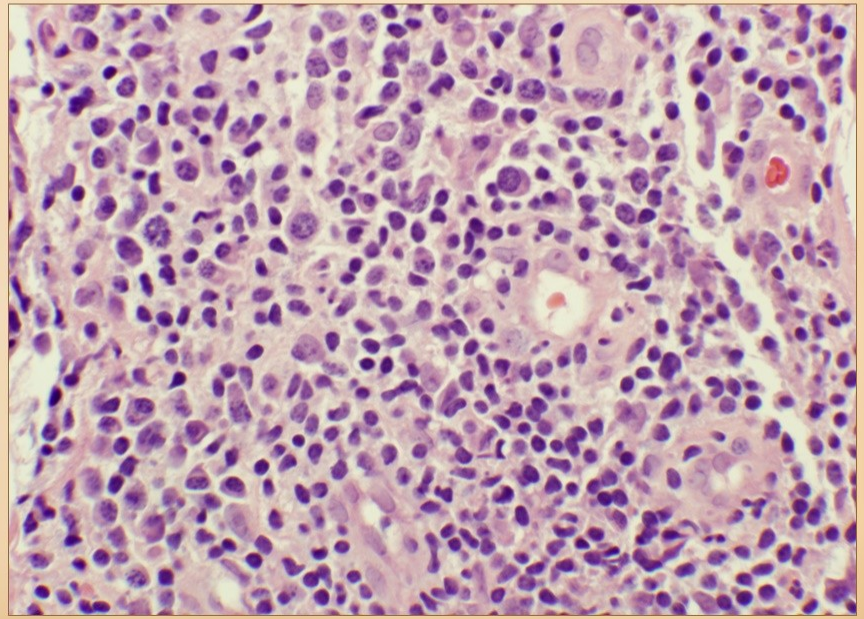

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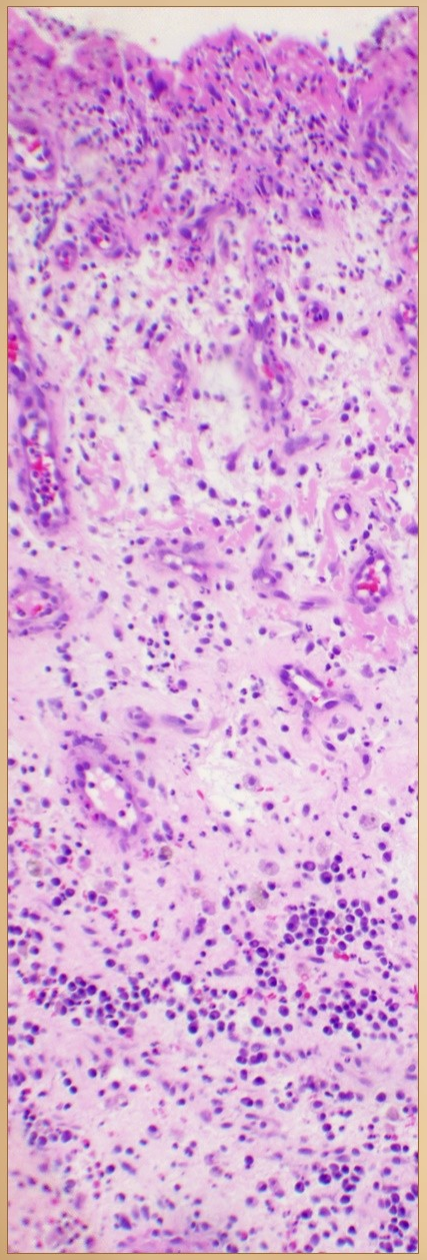

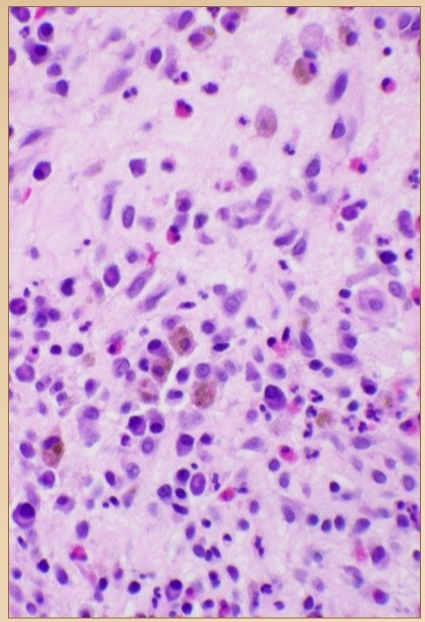

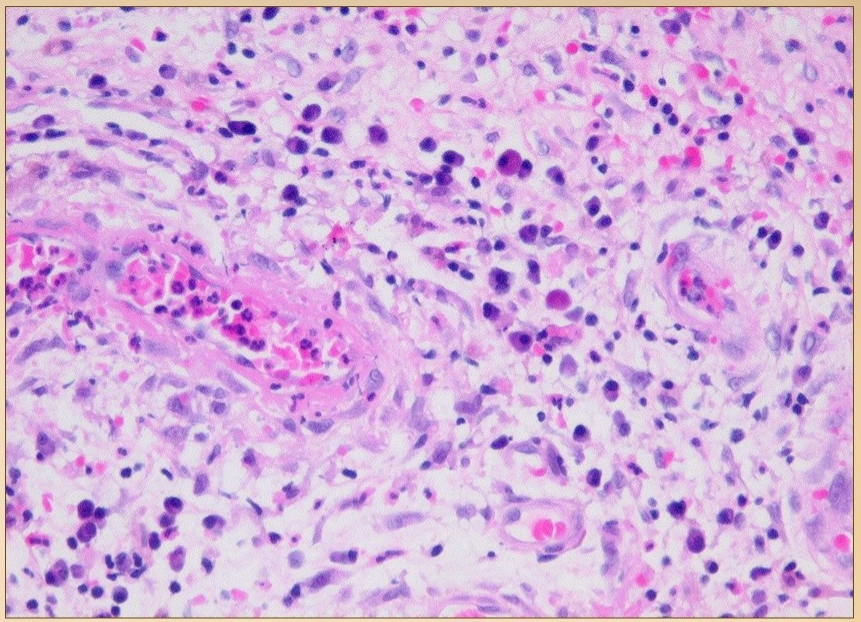

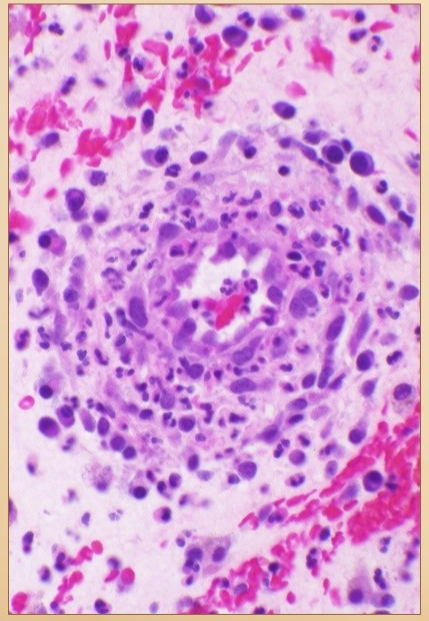

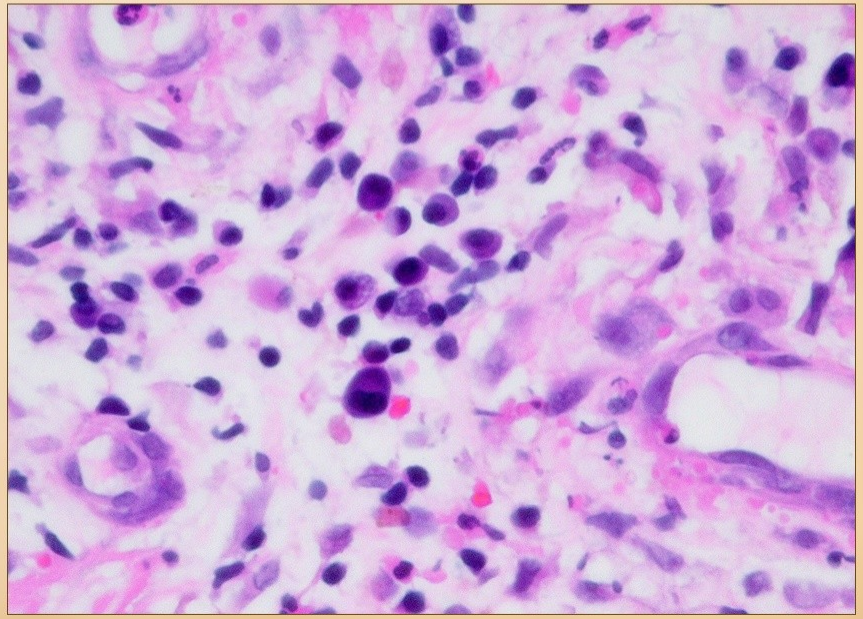

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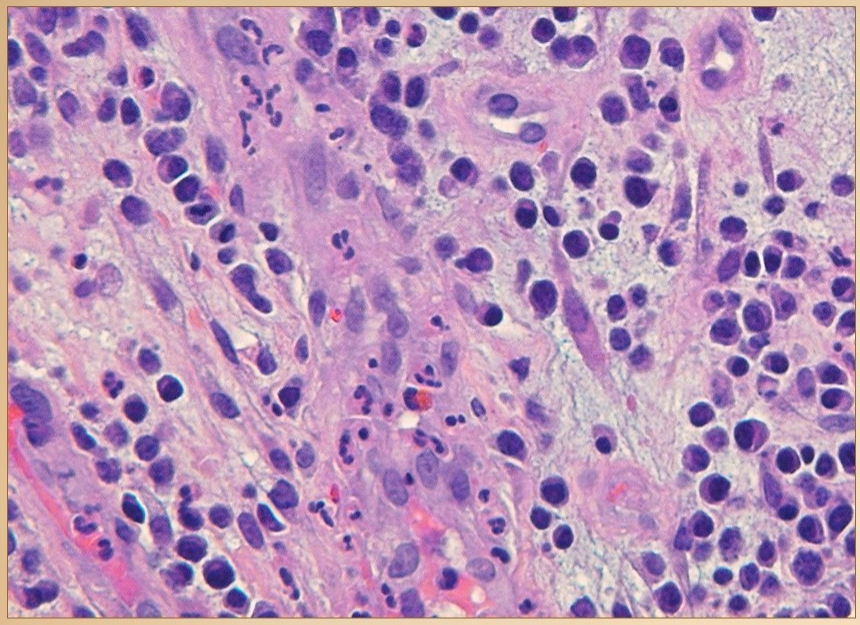
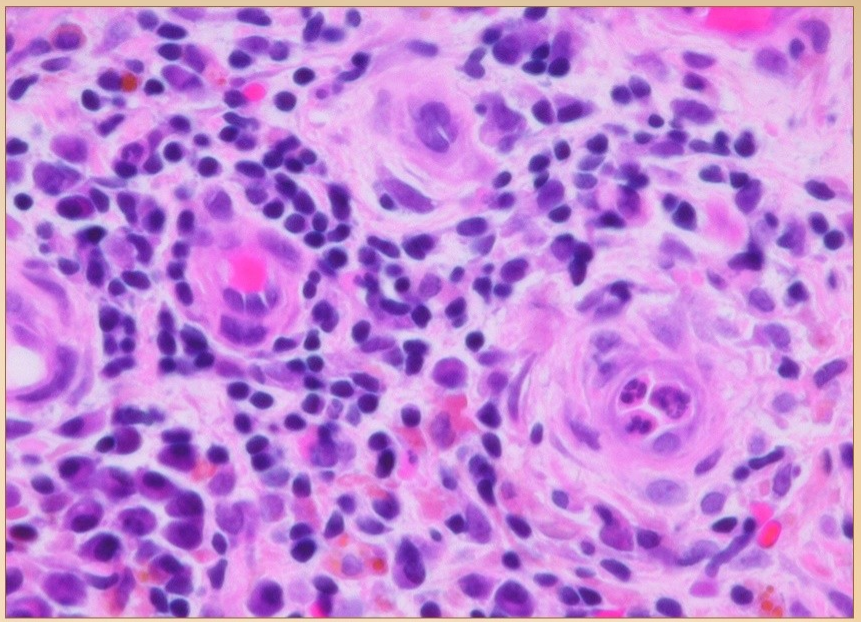
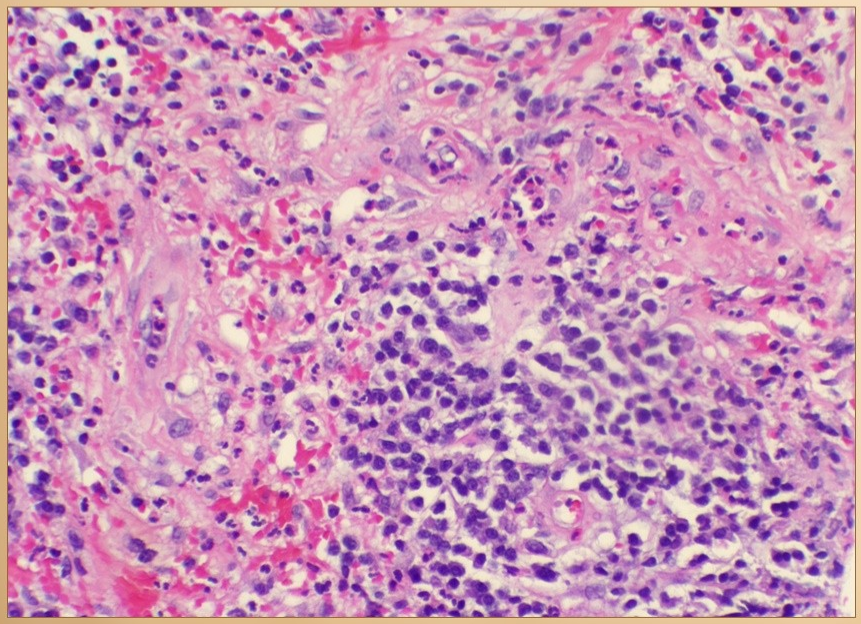
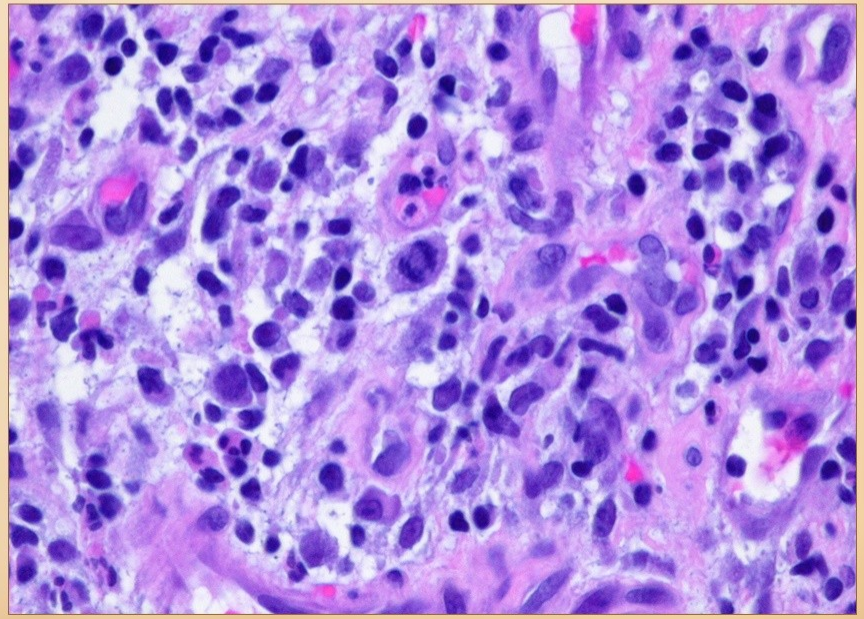






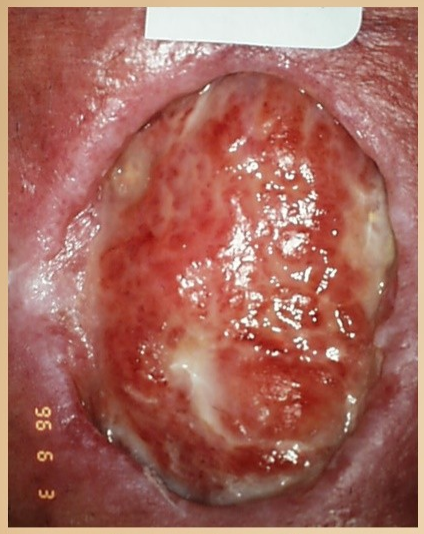


DYSDYNAMIA -VS- DISEASE

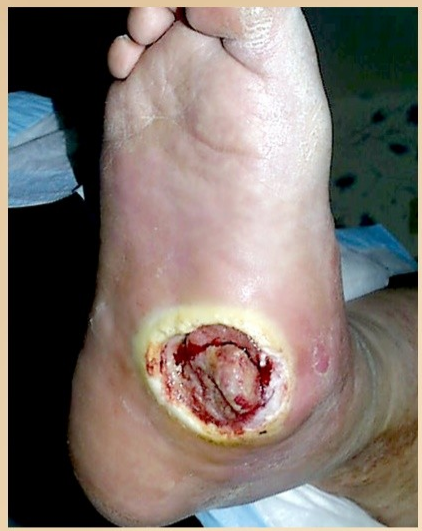
NOT ALL CHRONIC WOUNDS ARE INTRINSICALLY CHRONIC & PATHOLOGICAL

Here are examples where non-healing is due to identifiable extrinsic pathologies of control loop elements and operations

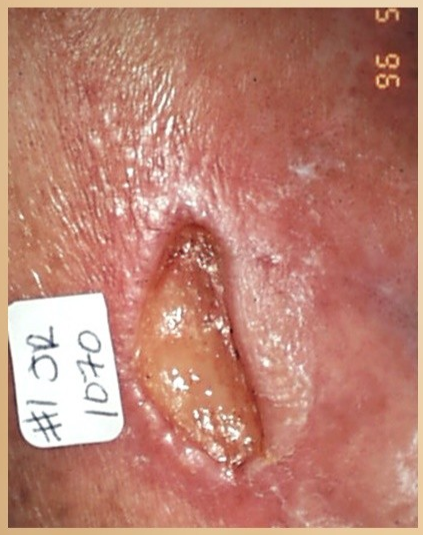
as opposed to when everything in the loop is nominally normal, but not cooperating or organizing due to population & dynamical chaos.



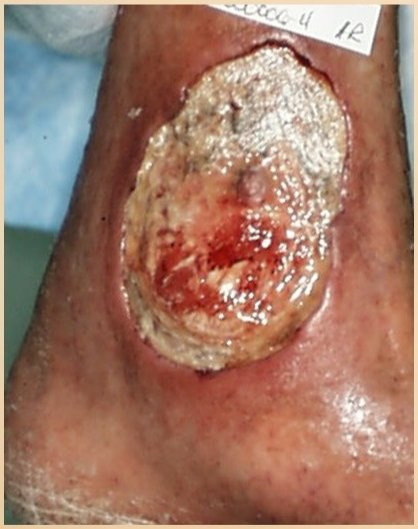
OPEN TENDON



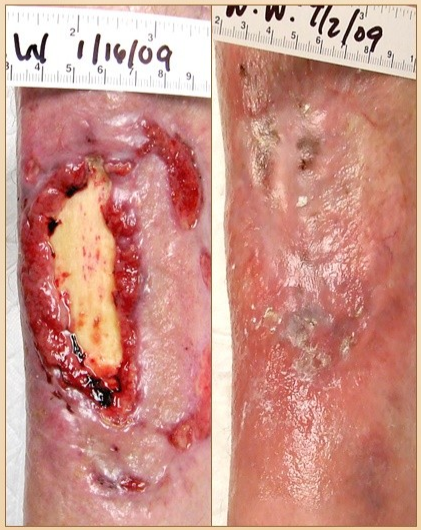
PRESSURE,
OPEN JOINT



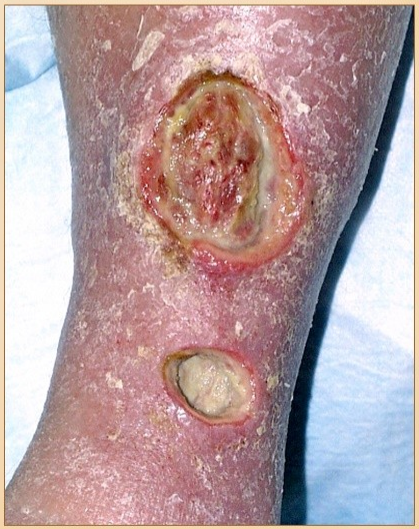
CHEMOTHERAPY



RADIATION



ARTERIAL



IATROGENIC,
CHEMICAL INJURY

THE PHYSICS AND PATHOLOGY OF WOUNDS

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Marc E. Gottlieb, MD, FACS

Phoenix, AZ

1

The Wound as a System and a Controlled Machine

The wound module, the wound control loop, wound pathology, and the basic dynamics of healthy and impaired wounds.

2

Auto-Immunopathy and the Intrinsic Disease of Wound Healing

The cellular and histopathological basis of intrinsic wound failure & wound chronicity: chronic inflammation, wound autoimmunopathy, and the 3-population wound.

3

Chronicity and the Physics of Wound Failure

The physics of wound failure and chronicity: N-body dynamics and chaos, population logistics, cellular automata and self-organization.

CHRONICITY, CHRONIC INFLAMMATION, & THE PHYSICS OF WOUND FAILURE

All systems - physical, biological, natural, engineered - must obey basic physical laws and relationships, e.g.
Thermodynamics - Conservation - Newton - Ohm - Maxwell - Physical Chemistry - Mathematics

ORGAN	STRUCTURE & FUNCTION	FAILURE	PHYSICS
HEART	*pump, valves, & pipes*	*chf = inadequate pump*	*fluid mechanics*
KIDNEY	*filter & resorption membrane*	*occluded filter*	*hydraulics & ionic chemistry*
LUNG	*bellows & diffusion membrane*	*faulty ventilation & respiration*	*gases & diffusion*
EYE	*light collector & detector*	*blindness*	*optics*
WOUND	*cell set & self-re-organization*	*logistical disorganization*	*populations, dynamics, automata*

THE WOUND MODULE IS A SPECIAL AD HOC RESERVE ORGAN

What are the quintessential structures and functions of the wound ?
It is a collection of mutually interactive self-organizing cell populations.
It has no other function than to organize itself,
into a generic stroma to support epithelium and other tissues.

What is the quintessential derangement of intrinsic wound pathology and chronicity ?
It is a dynamical disorder of logistical self-re-organization among these populations.
When it fails, it simply fails to organize to its intended final form,
to complete its task to become something and then disappear.

What are the fundamental physics relevant to the wound ?
Non-linear dynamics, control, chaos, population logistics, cellular automata.
It is the science of populations, their interactions, control, and self-organization.
When it fails, it is a dynamical disorder of self-organizing populations.

THE PHYSICS & PATHOLOGY OF WOUNDS - 3

CHRONICITY & THE INTRINSIC DISEASE OF WOUND HEALING

THERE ARE FEW INBORN ERRORS OF WOUND HEALING.

WHAT THEN IS THE INTRINSIC PATHOLOGY OF THE WOUND?

It is a state of autonomy or self-perpetuation
not contingent on the primary pathology.

IT IS A DYNAMICAL DISORDER OF A COMPLEX SYSTEM DUE TO:

continued primary disease,
injury, inflammation, thrombosis

chronic inflammation - the 3rd population

population dependencies and feedbacks that sustain
thrombosis, inflammation, & dynamical disorganization

a stable attractor & thermodynamic basin

Primary disease, injury, inflammation, thrombosis can have a crucial
role in perpetuating the early wound and in inducing chronic inflammation.

To the extent that they continue, then the pathological
non-healing state remains stronger and harder to break.

However, once the third population and dynamical dependencies and attractors
have settled in, then primary pathology is no longer needed to sustain the problem.

The wound can then persist even when good care has resolved acute stressors.
The inherent dynamical stability of this state resists further treatments.

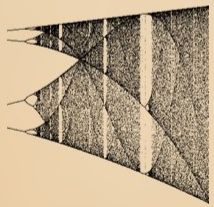

END

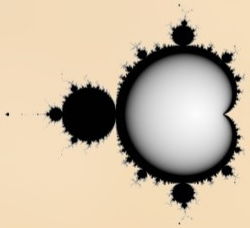
The Physics and Pathology of Wounds. Part 3.
Chronicity and the Physics of Wound Failure.

Marc E. Gottlieb, MD, FACS Phoenix, AZ

The wound module is a transient set of interacting cells which collectively restore in-jured tissue to normality, a fibrous stroma of angiocytes and fibroblasts. Its healthy aggregate behavior is a well behaved machine, governed by the physics of control systems. A sick system can result from various extrinsic perturbations, but the core mechanism of self-sustaining persistent dysfunction, the true intrinsic disease of wound healing is chronicity itself, the paramount cause being wound module autoimmunization. This state is disruptive but not fully toxic or lethal, thus immunopathic wounds have complex behaviors, at times better-worse-stable-variable, often looking healthy, but always frustrating as they refuse to cross the finish line. How does one explain such variable behavior and the differences between normal and chronic-and-pathological (cap) wounds?

Simply stated, intrinsic wound pathology and chronicity is a dynamical disorder of complex populations. The physics governing complex behaviors in complex systems is ***non-linear dynamics*** (nld). In addition to ***control***, three aspects of NLD are especially important to wound pathology. (1) ***Population logistics***. Healthy healing is a sequence of one-shot self-completing linear events: primary injury & thrombosis –*then*– acute inflammation –*then*– wound module. Pathology creates abnormal population dependencies (nutrition, starvation, predation, cultivation) and a new population, chronic inflammation. Non-linear perpetual complexity arises in the logistics of injury & thrombosis –*vs*– acute inflammation –*vs*– wound module –*vs*– chronic inflammation –*vs*– injury & thrombosis. (2) ***Cellular automata & self-organization***. The "cellular" agents of the wound module (real biological cells in this case) have a small set of deterministic rules of interaction with each other. When allowed to function properly, stromal rebuilding is automatic and correct. Under pathological conditions, self-organization, i.e. wound healing is disrupted. (3) ***Chaos & N-body dynamic***s. The net effect is that the wound, a set of several interacting cell populations, has 3 attractors (basins, dynamically stable states or behaviors): convergence (healing), divergence (ulcerating), and self-sustained chaotic orbits (chronicity).





*Basic methods to demonstrate non-linear dynamics: l**eft**, the logistical map of competing populations; **middle**, diffusion-limited-aggregation, an example of self-organizing automata; **right**, attractors and chaos in the Mandelbrot set of complex-plane iteration. While seemingly abstract, these structures are directly correlated with wound events.*

Marc E. Gottlieb, MD, FACS
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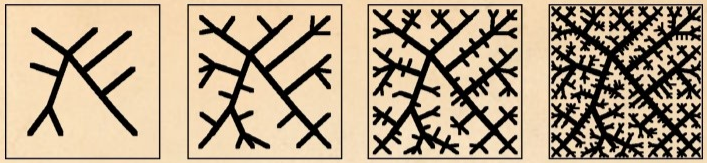

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The Physics and Pathology of Wounds. Part 3. Chronicity and the Physics of Wound Failure.

Original presentation February 22-26, 2010, Maui, Hawaii
at the
John A. Boswick, M.D. Burn and Wound Care Symposium

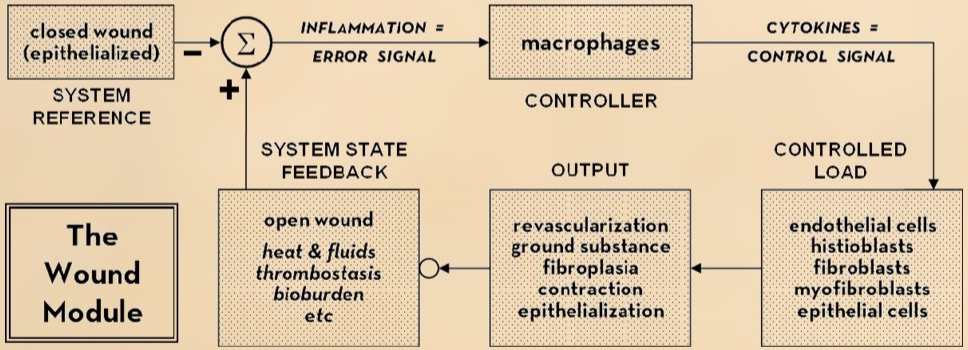
The presentation and related materials can be viewed and used at:
arimedica.com

The Physics and Pathology of Wounds. Part 1.
The Wound as a System and a Controlled Machine.

Marc E. Gottlieb, MD, FACS Phoenix, AZ

The wound is a transient organ of inter-operating cells, triggered into being by injury and inflammation, then extinguishing as it completes its repair of injured stroma. It is a system. Conventional bioscience tends to characterize properties and interactions of individual or one-versus-another elements within a system, but physics is required to understand the integrated timewise behavior of whole systems. Intrinsic wound pathology and chronicity, and wound failure and therapeutics are easily explained when wounds are seen as a ***non-linear System*** (rather than as a collection of dual-element linear interactions). For normal wound physiology and for the pathophys-iology of altered and failing wounds, the governing principles are the physics of complex systems: non-linear N-element dynamics, control science, population logistics, and self-organizing automata.

Understanding wound physics begins by characterizing normal wound physiology. The wound is a closed-loop reference-driven non-linear multicontrol system. Sick and altered wounds have layers of added complexity, but the quintessential intrinsic machinery of wound healing – the ***Wound Module*** of post-inflammatory wound repair – functions as just a single control loop. When tissues are injured, the ***Main Control Loop*** of physiological wound repair will drive cells to reorganize back to a repaired stroma.

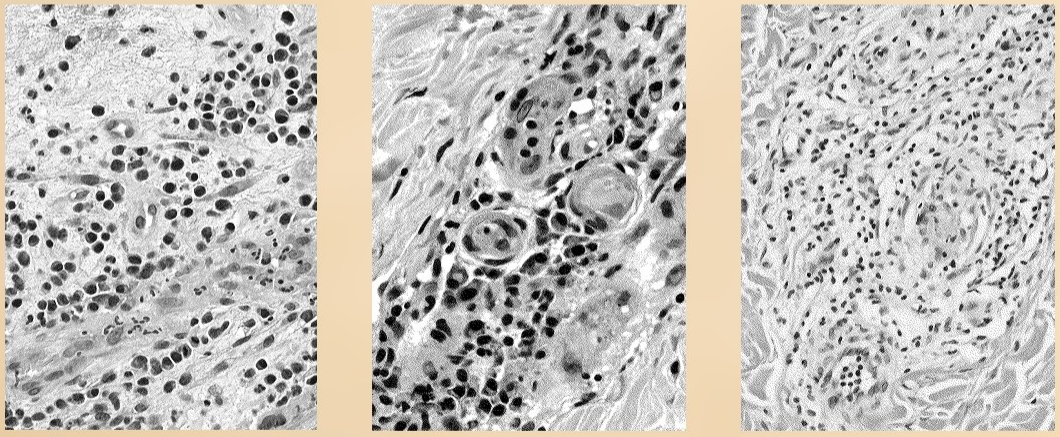


The wound control system is composed of these elements: The ***system state*** is the open wound and its conditions. It is compared (Σ) to a ***reference***, normal epithelialized tissue. Variances generate an ***error signal*** in the form of inflammation. This activates macrophages which are the ***system controller***. They in turn generate a ***control signal*** in the form of cytokines. The ***controlled load*** is the group of local responder cells. Their ***output*** are the elements of histogenesis, which modify the state of the system, which then feeds back to the loop at the summing point. Any discussion or research of the collective behavior of a wound must acknowledge this basic control system.

The Physics and Pathology of Wounds. Part 2.
Auto-Immunopathy and the Intrinsic Disease of Wound Healing.

Marc E. Gottlieb, MD, FACS Phoenix, AZ

Many chronic wounds result from disorders extrinsic to the healing process, e.g. pressure or arterial disease. What then are the intrinsic diseases of wound healing? Compare the wound to other organs. The quintessence of heart failure is that it is an inadequate pump, for lung failure it cannot exchange gases. But the wound is neither pump and pipes, nor bellows and diffusion membrane, nor is it like any organ with macro-anatomical structure. It is a transient collection of mutually interacting self-organizing cells. Stromal angiocytes and fibroblasts (wound cells) have remarkably few inherent metabolic or genetic faults. Dysfunction of the aggregate population is almost always the result of deprivation or predation. Adverse states can be caused by (1) non-targeted exogenous conditions such as arterial ischemia or repetitive trauma, and (2) targeted damage directed against these cells and their structures. As will be presented here, predation against the wound module is due to a state of auto-immunopathy in which lymphoid cells are sensitized to wound components. Not only does this occur with classic connective tissue disorders and other well-recognized auto-immunopathies, but it happens when a wound becomes intrinsically chronic and pathological. Hypercoagulability and other conditions of persistent thrombosis and acute inflammation are the underlying states that induce the auto-immunization. Simply put, intrinsic wound pathology and chronicity is a dynamical disorder of complex populations caused by auto-immunopathic disruption of the wound module.



*In these chronic non-healing wound samples, the vascular locus is infiltrated with immune cells (**left**, plasma cells; **middle**, plasma cells and eosinophils; **right**, lymphocytes.) On the left, plasma cells are mixed with the migratory angiocytes (spindles) that are trying to assemble the wound. At middle and right, chronic thrombosis due to a primary hypercoagulable disorder is not only present, it is the root cause of this entire state.*

The Physics and Pathology of Wounds. Part 3.
Chronicity and the Physics of Wound Failure.

Marc E. Gottlieb, MD, FACS Phoenix, AZ

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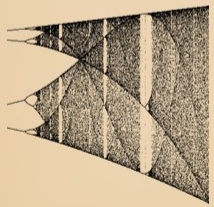

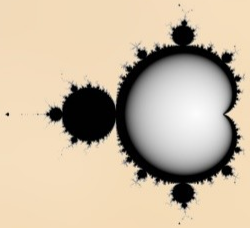

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