Multi-Scale Modeling in Computational Surgery: Application to Breast Conservative Therapy

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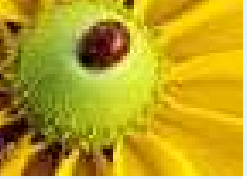


Computational ≠ Surgery

Surgery Manipulation in 8 words

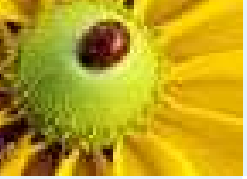
(1) Exploration, (2) Aspiration/Injection, (3) Incision (4) Excision, (5) Evacuation, (6) Extraction, (7) Scarification, (8) Closure.

Modern Surgery enabled by computational science and technologies

- Augmented Visualisation
- Augmented Manipulation
- Active tracking devices
- Prosthesis
- Individualized procedural planning and rehearsal

Surgeons and Computational Scientist leave in different worlds

- ≠ Vocabulary and Concepts
- ≠ Objectives
- ≠ Time Lines and Schedules

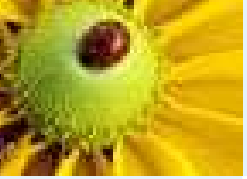


Computational Surgery: One Definition?

Computational surgery is the application of mathematics and algorithm design, enabling imaging, robotics, informatics, and simulation technologies, incorporating biological and physical principles, to improve surgery.

Computational surgery must reunite:
Interdisciplinary sciences
Integration of multiple technology
Immersed in surgery practice
Ethical Principles

To summarize IIIE !!! i.e not quite IEEE.....



Key observation

Today Silent Revolution from analogical to digital manipulation !

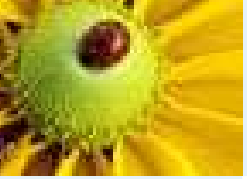
Enough digital info from

- Imaging
- Procedural guidance
- Virtual reality
- Physiological data
- Molecular data
- DNA data

to

- analysis on a case by case basis,
- data mind of large date base of clinical cases
- extract "medical" patterns in a systematic and rigorous way

All tools and method of information technology, mathematics and statistic are applicable to surgery problem.



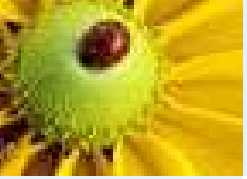
Predicting Surgery Outcome ?

Breast conservative therapy is a peculiar example of computational surgery:

- No specialized instrumentation
- No robots
- No complex anatomy
- Limited procedural options

Some of the challenges:

- Mobile structure
- Positional variation
- Image guided precision of surgery; lack of landmarks
- Intra-operative assessment of negative margins
- Elimination of in-breast recurrences: Incorporate adjuvant therapies
  - ☐ radiation
  - ☐ wound healing
- Prediction of cosmetic outcome
- Procedural planning



Objectives of Model and Simulation

- In Silico Methods may elucidate mechanism:
  - ☐ requires experimental data
- Added value to Clinical Trial protocol:
  - ☐ requires robust methods and computational infrastructure
- Patient specific predictive tools:
  - ☐ requires verification, validation, estimate of uncertainties.
- Surgery planning:
  - ☐ requires human computer interface

Fascinating area where interdisciplinary collaboration between computational scientist and MD is the key to success

3D Image Base Simulation - Short Time Scale

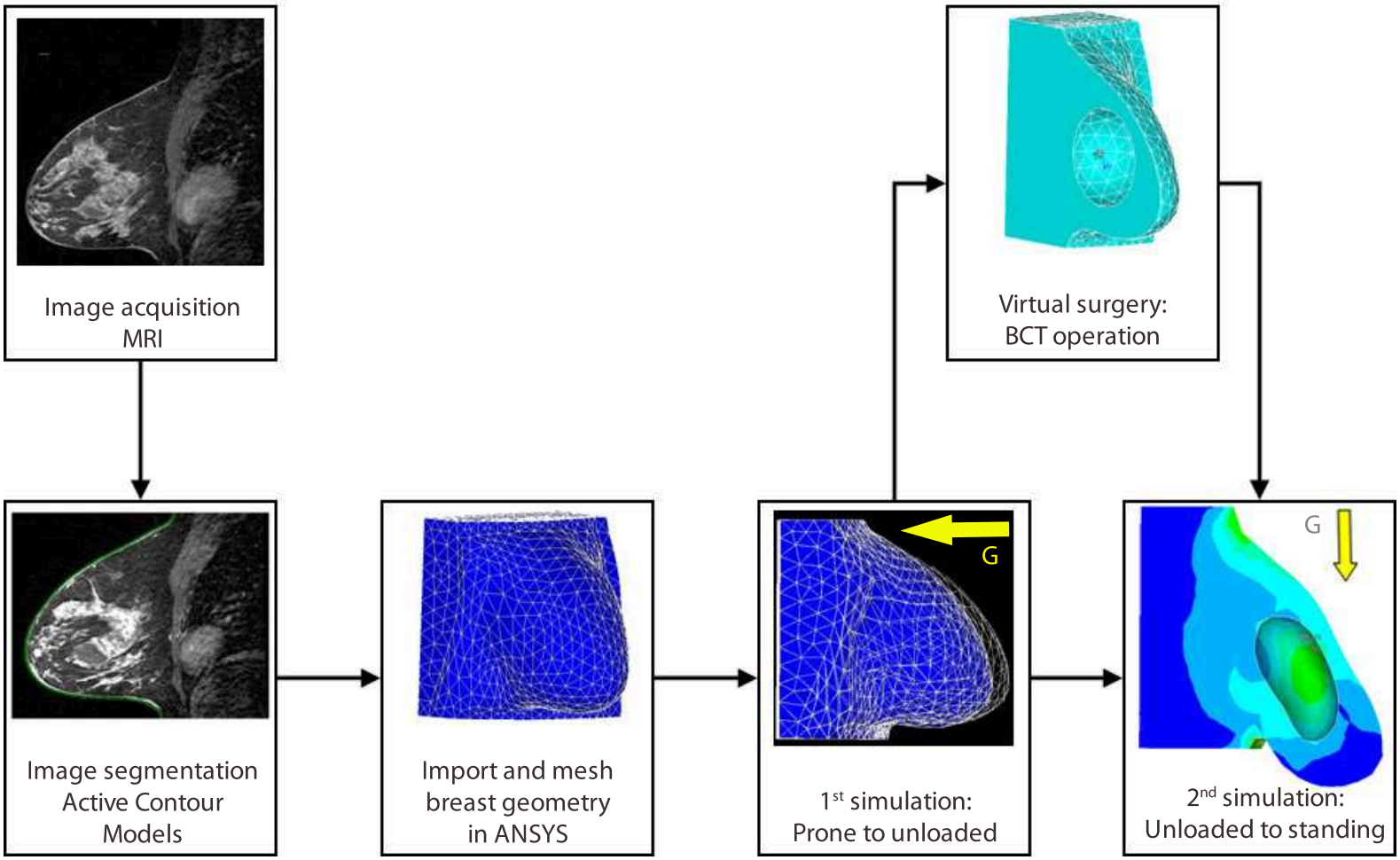


Image Analysis

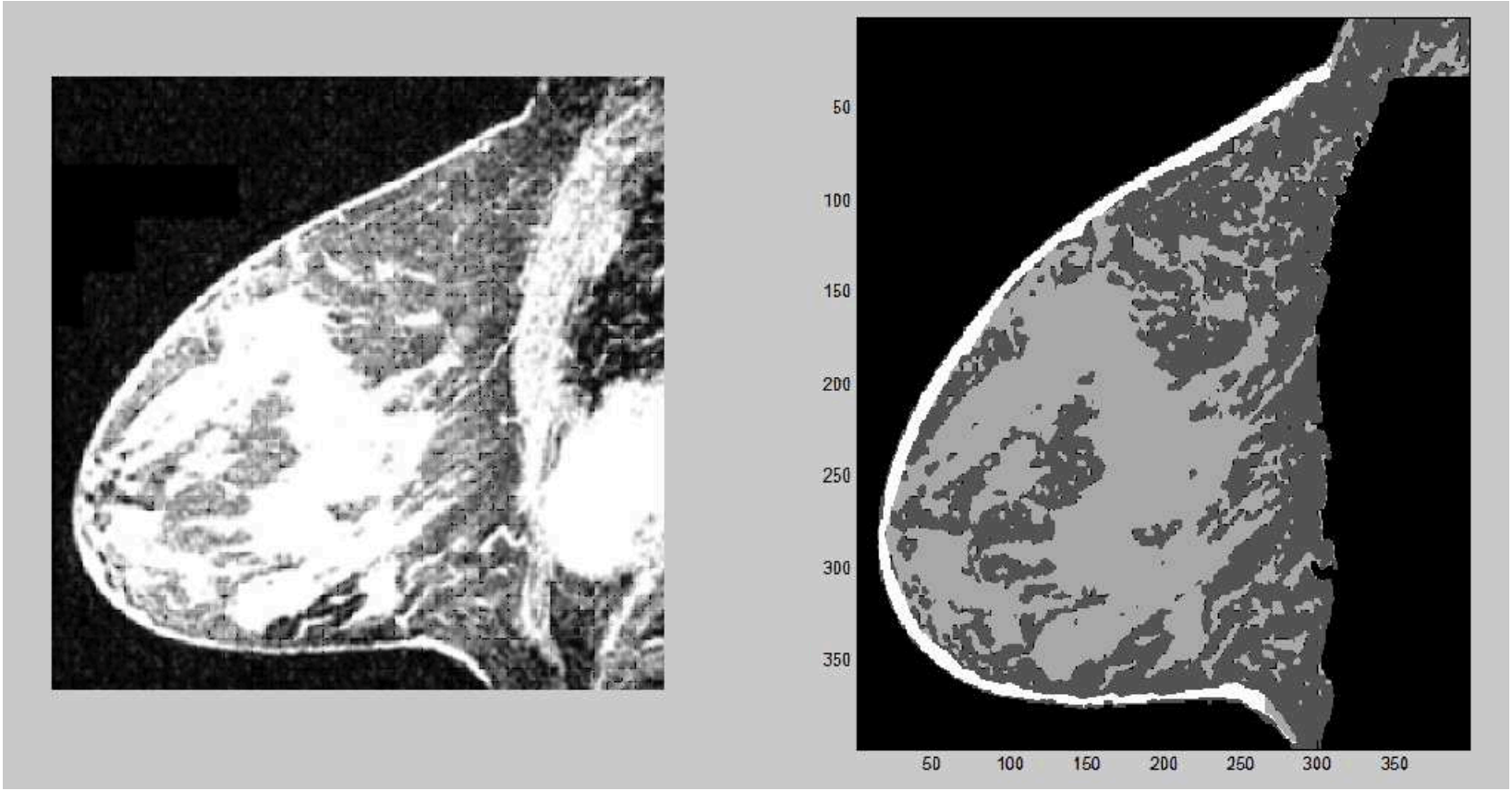


Figure 1: *Image Segmentation + Classification*

Two Time Scales Model

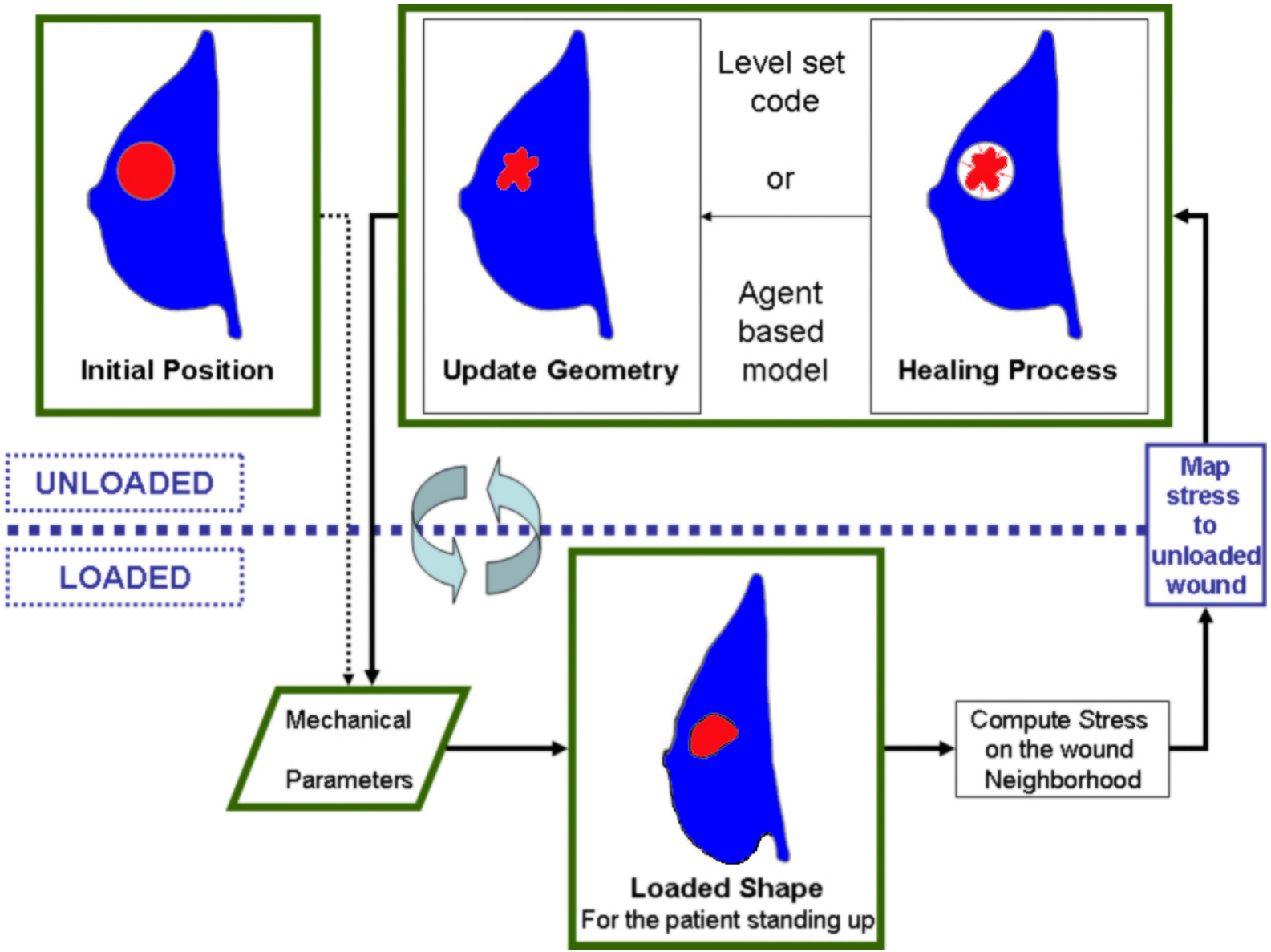


Figure 2: *Illustration of the two steps Algorithm.*

Level Set Scenario - Bridging scales

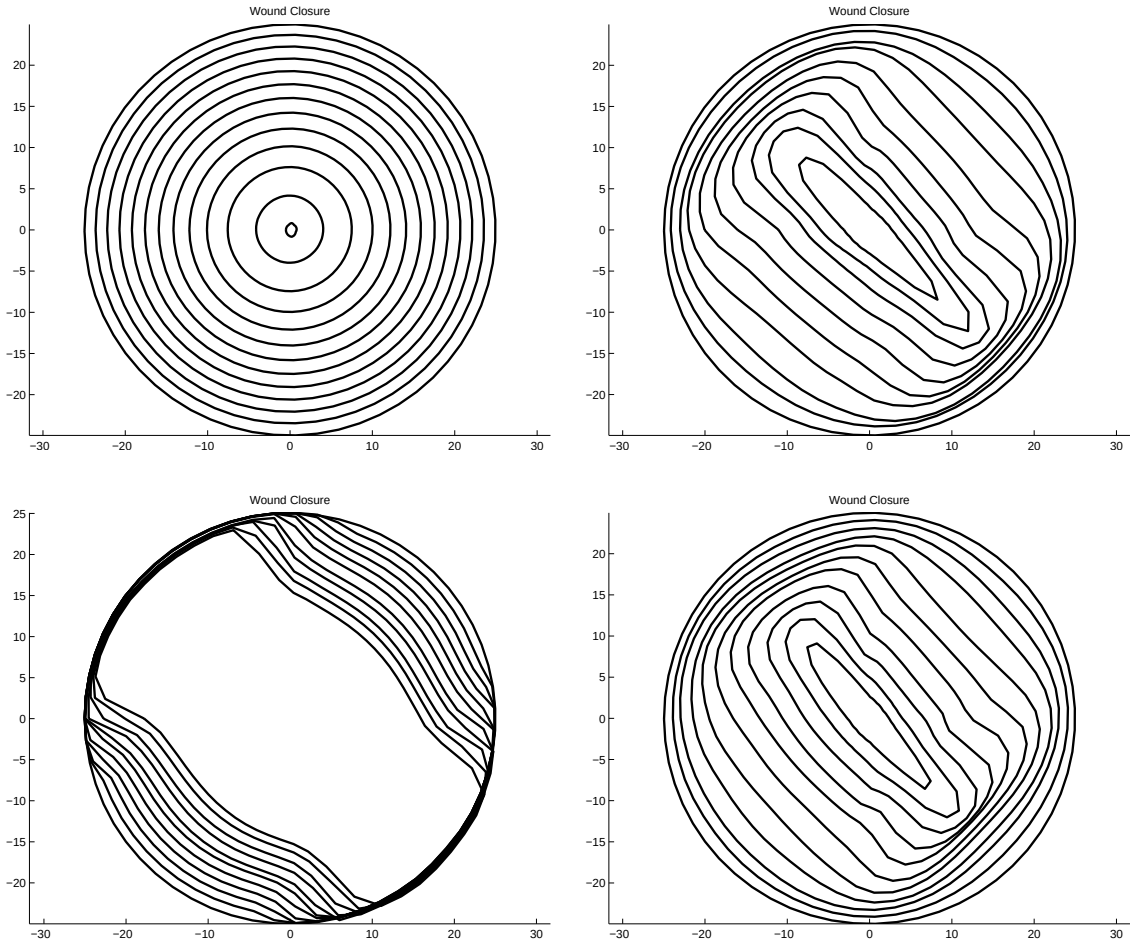
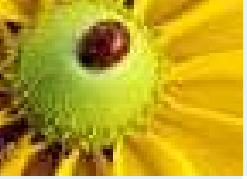


Figure 3: Wound history - reference shape at zero load from left to right wound history (i) driven by wound local curvature, (ii) driven by local strain energy strain, (iii) dominated by local lack of EGF, (iv) with weak dependence on EGF.



Agent Base Model

Bottom up approach with modeling at the cell level

- Explicit mapping of cells to space location.
- Basic set of rules to drive cell division, apoptosis, extra cellular matrix production/degeneration
- Production/Absorbtion of key molecules + diffusion
- Random walk of macrophage
- Motion of cells driven by gradient of some "concentration"
- NEW: Mechanical environment set up
- NEW: Multi-scale
- Possibly Angiogenesis -ref Peirce et Al.

ref-review: M.Hwang, M.Garbey, S.A. Berceli and R.Tran Son Tay, Cellular and Molecular Bioengineering, 2009.

Multi-scale prediction?

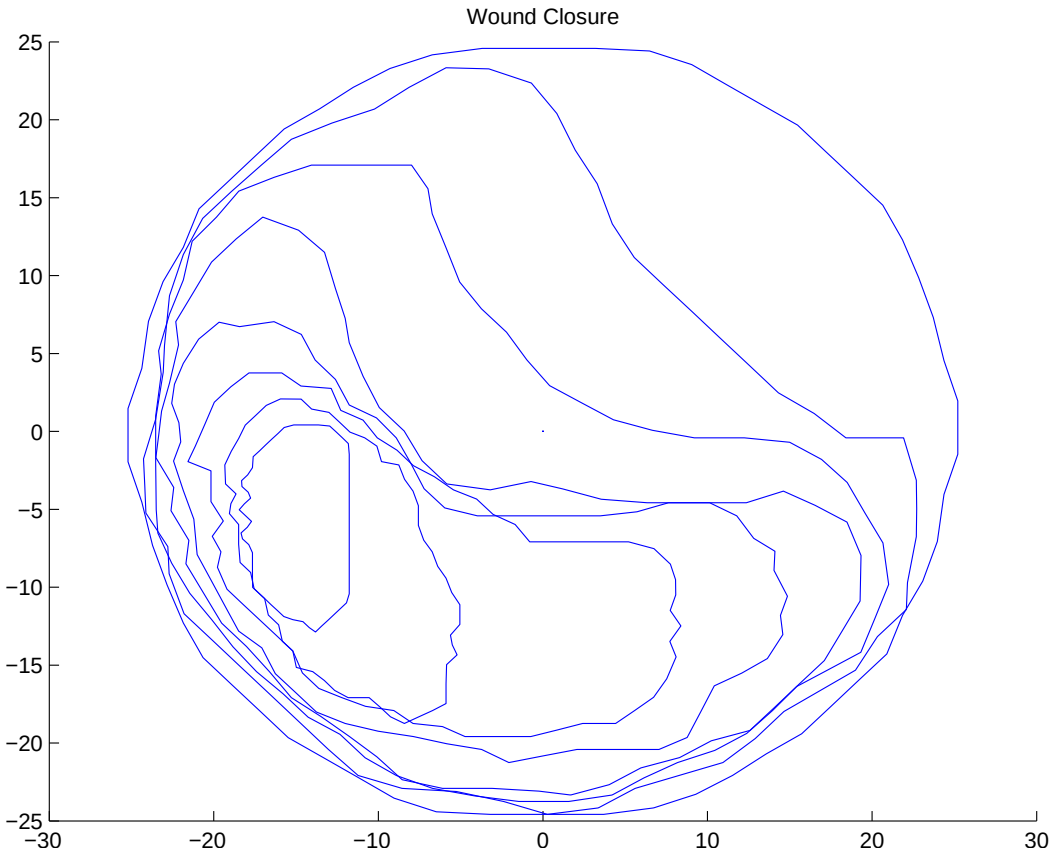
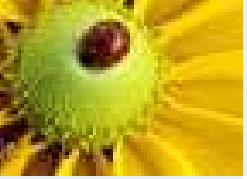


Figure 4: closing of the wound with the CA: rate of mitosis depending on local strain energy

While this CA model can match the level set prediction in some simple "regular" situation, one get new interesting patterns that one should be able to compare against clinical data.



Next Step

- Pilot clinical study: post surgery follow up with 3d ultrasound - MRI - patient feedback - ...

- Fit Multi-scale model
  - ☐ Understand Fundamental Mechanisms by "Reduction Method" using Non Linear Optimization Algo.
  - ☐ Calibrate Surrogate Model Toward Clinical Prediction.

- Run hybrid PDE-CA system with $O(10^{11})$ cells thanks to parallel computing.

- Add Biology as needed, thanks to lab experiments: lack of animal models for BCT.

"Rather Universal Approach that deserve a general theoretical/computational infrastructure for clinical trial"
see for example work with Scott Berceli and Roger Tran Son Tay on vein graft

Final Objective: Tool Box ?