Module 1: Active Contours... Segmentation and Tracking

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The future includes in vivo cellular and molecular imaging. This imaging will benefit our understanding of mechanisms and pathways.

-- (paraphrase) Elias Zerhouni, former NIH Director
This first part of the module

- Explains how to make an active contour ("snake")

- It should be accessible to anyone with high school calculus! (The first module is a bit heavier on the mathematical explanation as compared to the following three)

Segmentation

- Is the processing of dividing an image into its constituent homogeneous regions

- Example: find the closed boundary of cell
**Segmentation**
- Is easier said than done.
  - It’s hard to get a closed contour
    - Linking edges...
  - It’s hard to make a smooth closed contour
  - It’s even harder in 3D (not really treated in this tutorial)

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**Parametric Active Contour Model**

\[
E_{\text{snake}} = \frac{1}{2} \int_{0}^{1} \left\{ \alpha \left( \frac{dC(s)}{ds} \right)^2 + \beta \left( \frac{d^2C(s)}{ds^2} \right)^2 \right\} ds + \int_{0}^{1} E_{\text{ext}}(C(s)) ds
\]

- Internal energy of the snake
- External energy, computed from Image

\[C(s) = (X(s), Y(s))\]
- is a snake point or snaxel and \(\alpha, \beta\) are weighting parameters.

Kass, Witkin, Terzopoulos, 1987
Parametric contours

A snake point / snaxel: \((X(s), Y(s))\)

Let’s
- See if we can make it through the next two *ugly* slides.
Variational Method

We have: \[ E_{\text{snake}} = \frac{1}{2} \int_0^1 F(C, \frac{dC}{ds}, \frac{d^2C}{ds^2}; s)ds \]

We want: \( C(s) \) that minimizes the above

Variational Step-- Vary \( C(s) \) slightly: \[ C(s, \varepsilon) = C(s) + \varepsilon \Phi(s) \]

where \( \Phi(0) = \Phi(1) = 0 \)

We can show that (see “variational proof” in appendix):

\[
\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial \varepsilon} = \frac{1}{2} \frac{\partial}{\partial \varepsilon} \int_0^1 \left[ C(\varepsilon, s) \frac{dC(\varepsilon, s)}{ds}, \frac{d^2C(\varepsilon, s)}{ds^2}; s \right] ds \\
\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial \varepsilon} = \frac{1}{2} \frac{\partial}{\partial \varepsilon} \left[ \frac{\partial F}{\partial C} - \frac{d}{ds} \frac{\partial F}{\partial C'} + \frac{d^2}{ds^2} \frac{\partial F}{\partial C''} \right] \Phi(s) ds
\]

Look at this part – we want the entire expression to be zero… why?

Variational Method

So, now we have a condition for \( E \) to be a minimum:

\[
\frac{\partial F}{\partial C} - \frac{d}{ds} \frac{\partial F}{\partial C'} + \frac{d^2}{ds^2} \frac{\partial F}{\partial C''} = 0
\]

This gives us the Euler equations (see “Variational Solution” in appendix):

\[
\frac{\partial}{\partial x} E_{\text{ext}}(X(s), Y(s)) - \alpha \frac{d^2X(s)}{ds^2} + \beta \frac{d^4X(s)}{ds^4} = 0 \\
\frac{\partial}{\partial y} E_{\text{ext}}(X(s), Y(s)) - \alpha \frac{d^2Y(s)}{ds^2} + \beta \frac{d^4Y(s)}{ds^4} = 0
\]

And the snake position update equations:

\[
X_{t+1}(s) = X_t(s) - \Delta t \left[ \frac{\partial}{\partial x} E_{\text{ext}}(X(s), Y(s)) - \alpha \frac{d^2X(s)}{ds^2} + \beta \frac{d^4X(s)}{ds^4} \right] \\
Y_{t+1}(s) = Y_t(s) - \Delta t \left[ \frac{\partial}{\partial y} E_{\text{ext}}(X(s), Y(s)) - \alpha \frac{d^2Y(s)}{ds^2} + \beta \frac{d^4Y(s)}{ds^4} \right]
\]

These equations make the snake move!
Example of external energy

The snake wants to exist where gradient magnitude is high – on the cell boundary

Edge energy:

\[ E_{\text{ext}}(C(s)) = -\left| \nabla \left( G_\sigma(x,y) * I(x,y) \right) \right| \]

Gradient operator Convolution

Problem: if my initial snake is away from the cell edge, the snake can’t “see” the gradient and can’t lock onto the edge…

A Snake Tracker

A combination of active contour models used for segmentation and the cell tracking techniques
The second part of this module

- The Tracking Problem
- Focus on active contour external forces
- Stabilization / Moving field of view
- Initialization of tracking / Detection and tracking of cells

- And we’re not done with active contour segmentation yet!

An example problem

Automated detection and tracking of rolling leukocytes (activated white blood cells) from intravital microscopic video imagery

Why? Rolling leukocyte flux / velocity is an indicator of the inflammatory response (needed in basic inflammatory disease research and in drug validation)

Cell tracking involved in many other pre-clinical assays:
- Leukocyte migration in vitro
- Epithelial/endothelial cell migration
- Cancer cell adhesion under flow
Challenges

- Moving background
- Deforming leukocytes
- Image clutter
- Contrast change

We’ll discuss

- Tracking
- Detection

Intravital is tough!

In vitro

In vivo
Active Contours / Snakes

I image

II edge map

III external force

IV deformation

Active Surfaces

I image

II edge map

III external force

IV deformation
Shape-size Constrained Snake for Leukocyte Tracking

Shape-size constrained energy functional:

- Shape
- Size
- Position (minimize motion orthogonal to flow)


A Radial Snake Model for Tracking

Proposed radial snake energy functional:

\[ E_{\text{snake}}(P, Q, R) = E_{\text{edge}}(P, Q, R) + \mu_{\text{cons}}E_{\text{cons}}(R) + \mu_{\text{pos}}E_{\text{pos}}(P, Q, R) \]

\[ E_{\text{edge}}(P, Q, R) = \frac{1}{L_0} \int_0^{2\pi} \sum w(P + R(t) \cos(t), Q + R(t) \sin(t)) R(t) \, dt \]

\[ E_{\text{cons}}(R) = \frac{1}{2} \int_0^{2\pi} (R(t) - \rho)^2 \, dt \]

\[ E_{\text{pos}}(P, Q, R) = \frac{1}{2} (Q - P_0)^2 \]

where, \( L_0 = \int_0^{2\pi} R(t) \, dt \)

- Fewer weights – two weights can be selected by minimax method
Capturing Leukocyte by Shape-size Constrained Snake

Failure of snake without shape-size constraint
Snake successfully captures leukocyte with shape-size constraint

Role of shape and size constraints

Subimage
Only shape constraint
Only size constraint
Both constraints
White Contour – Initial
Black Contour – Final
Gradient Vector Flow (GVF)

Gradient Vector Flow: Diffusion of force vectors


Motion Gradient Vector Flow (MGVF)

- Idea: bias the external force vector field in the direction of motion – using acquired tracking information
Motion Gradient Vector Flow (MGVF)

MGVF energy functional:
\[ E_{\text{MGVF}}(w) = \frac{1}{2} \iint [H(w, (v^x, v^y)) |\nabla w|^2 + f(w - f)^2] dx dy \]

Minimization

\[ \frac{\partial w}{\partial t} = \text{div}(H(\nabla w, (v^x, v^y)) \nabla w) - f(w - f) \]

\( \nabla w \): Terned as MGVF and utilized as the edge force for the snake

A convergent numerical implementation is derived


Capturing Leukocytes With MGVF

MGVF snake with cell displacement less than \( \rho \)

MGVF snake with cell displacement more than \( \rho \)

MGVF snake can also move backward

\[ f = |\nabla | \quad (v^x, v^y) \text{: direction of leukocyte movement} \]

\( H \): heaviside function

Direction of cell movement
Tracking Examples

Implemented in real-time on Mercury system and NVIDIA GPU.
Can track 30 cells at 30 fps

Shape

Velocity, peeling angle and adhesion energy density
Moving Field of View Tracking

Challenge:
(1) Register frames
(2) Track

Automated Validation by Spatiotemporal Image

Tracker computed path in 3D (red) projection (blue) on 2D image domain
1D image columns (green)

Spatiotemporal image: A stack of rows

Frame number

Distance along track-path

Spatiotemporal track-path overlaid in red

Frame Height

Frame Width
Vector Field Convolution

- More recently, we have applied an external force called Vector Field Convolution (VFC)
- Idea: instead of diffusion (GVF), create external force vector field by convolving a vector field kernel with an edge map
- Advantages: faster, less sensitive to noise and clutter

Li Acton, *IEEE Trans. IP, 2007*
**Force Generation via Vector Field Convolution (VFC)**

\[ F_{VFC}(x,y) = \text{Edge Map} \ast K(x,y) \]

*\(K\) is a prefixed vector kernel with width, \(w\)

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**Leukocyte Detection (geometric approach)**

1. Score each ellipse by GICOV statistic: Gradient Inverse Coef. Of Variation – the mean outward normal component of gradient divided by the standard deviation
2. Use Bayesian threshold to determine which are cells...
Leukocyte Detection

We have shown that the GICOV score follows a non-central student t distribution. A Bayesian approach is used to determine when $P(\text{leukocyte}) > P(\text{non-leukocyte})$ for a given GICOV score. A snake is used to further refine boundary.

The general initialization problem

- We’ve shown examples of active contours for tracking and a method to initialize for cells.
- How to initialize in general so that active contours and surfaces can be used in generalized segmentation problems?
New Initialization

• Approach: View initialization as an inverse problem
• Fact: the boundaries of an object “cause” the external force vectors for a snake
• We attempt to estimate the boundary from the force vectors – inverse approach.

Poisson Inverse Gradient Approach

• Estimate the optimal external energy $E$ such that the negative gradient of $E$ is the closest vector field to $f$ in the $L_2$-norm sense,

$$E = \arg \min_E \int_{\Omega} \| -\nabla E - f \|^2$$
Solution – Poisson’s Equation

- Poisson’s equation

\[ \Delta E = -\text{div} \mathbf{f} \]

VFC field \( f_{\text{vfc}} \)

Poisson Inverse Gradient (PIG) Approach

- The minimum isocontour in \( E \) is our initial guess
- Solution to finding \( E \) is given by Poisson’s equation, so we call the method PIG: Poisson Inverse Gradient
- PIG
  - Accommodates broken edges / high curvature objects
  - Is Robust to noise
  - Accommodates multiple objects
  - Accelerates the active model convergence
Initialization for leukocyte tracking

**Conclusion**

- So that’s (one way of) how to segment and track cells with snakes!
Discretization

Using the Euler equation for \( X(s) \)...

\[
\frac{\partial}{\partial x} E_{\text{ext}} (X(s), Y(s)) - \alpha \frac{d^2 X(s)}{ds^2} + \beta \frac{d^4 X(s)}{ds^4} = 0
\]

This becomes (for one “snaxel”)

\[- f_x(X_i, Y_i) - \alpha (X_{i+1} - 2X_i + X_{i-1}) + \beta (X_{i+2} - 4X_{i+1} + 6X_i - 4X_{i-1} + X_{i-2}) = 0\]

In matrix form:

\[- f_x + AX = 0\]

So the explicit method is

\[X^{t+1} - X^t = \Delta t (f_x - AX^t)\]
Implicit Method

The explicit method is unstable for practical time steps $\Delta t$

$$X^{t+1} - X^t = \Delta t \left( f_x - AX^t \right)$$

The implicit method is given by

$$X^{t+1} = \left( I + \Delta t A \right)^{-1} \left( \Delta t f_x + X^t \right)$$

$$X^{t+1} - X^t = \Delta t \left( f_x - AX^{t+1} \right)$$

$$(I + \Delta t A)X^{t+1} = \left( \Delta t f_x + X^t \right)$$

Same form for $Y$...

Shape and Size Energy Terms

$$E_{\text{total}} = E_{\text{snake}} + \lambda_1 E_{\text{shape}} + \lambda_2 E_{\text{size}}$$

$$E_{\text{shape}}(X,Y) = \frac{1}{2} \left[ R_x(s, X(s)) - \bar{R}(X,Y) \cos(2\pi s) \right]^2 ds + \frac{1}{2} \left[ R_y(s, Y(s)) - \bar{R}(X,Y) \sin(2\pi s) \right]^2 ds,$$

$$E_{\text{size}}(X,Y) = \frac{1}{2} \left( \bar{R}(X,Y) - K \right)^2,$$ where

$$R_x(s, X(s)) = X(s) - \int_0^1 X(r) dr, \quad R_y(s, Y(s)) = Y(s) - \int_0^1 Y(r) dr$$

and $\bar{R}(X,Y) = \int_0^1 \sqrt{R_x(s, X(s))^2 + R_y(s, Y(s))^2} ds$. 
Variational Proof

\[
\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial \varepsilon} = \frac{1}{2} \frac{\partial}{\partial \varepsilon} \int_0^1 F \left[ C(\varepsilon, s), \frac{dC(\varepsilon, s)}{ds}, \frac{d^2C(\varepsilon, s)}{ds^2}; s \right] ds
\]

\[
= \frac{1}{2} \int_0^1 \frac{\partial}{\partial \varepsilon} F \left[ C(\varepsilon, s), \frac{dC(\varepsilon, s)}{ds}, \frac{d^2C(\varepsilon, s)}{ds^2}; s \right] ds
\]

Since limits of integration are fixed

\[
= \frac{1}{2} \int_0^1 \left( \frac{\partial F}{\partial C} \frac{\partial C}{\partial \varepsilon} + \frac{\partial F}{\partial C'} \frac{\partial C'}{\partial \varepsilon} + \frac{\partial F}{\partial C''} \frac{\partial C''}{\partial \varepsilon} \right) ds
\]

By the Chain Rule

\[
\frac{\partial C(\varepsilon, s)}{\partial \varepsilon} = \Phi(s)
\]

\[
\frac{\partial C'(\varepsilon, s)}{\partial \varepsilon} = \frac{\partial [C'(s) + \varepsilon \Phi'(s)]}{\partial \varepsilon} = \frac{\partial \Phi(s)}{\partial s}
\]

Using integration by parts

\[
\int_0^1 \frac{\partial F}{\partial C'} \frac{\partial \Phi(s)}{\partial s} ds = 0 - \int_0^1 \frac{d}{ds} \left( \frac{\partial F}{\partial C'} \Phi(s) \right) ds
\]

\[
= \int_0^1 \frac{d}{ds} \left[ \frac{\partial F}{\partial C} C + \frac{d^2}{ds^2} \frac{\partial F}{\partial C'} \Phi(s) \right] ds - \int_0^1 \frac{d}{ds} \left( \frac{\partial F}{\partial C'} \Phi(s) \right) ds
\]

\[
= \int_0^1 \frac{d}{ds} \left( \frac{\partial F}{\partial C} C + \frac{d^2}{ds^2} \frac{\partial F}{\partial C'} \Phi(s) \right) ds
\]

More Variational Method

Likewise:

\[
\frac{\partial C''(\varepsilon, s)}{\partial \varepsilon} = \frac{\partial^2 \Phi(s)}{\partial s^2}
\]

\[
\int_0^1 \frac{\partial F}{\partial C''} \frac{\partial \Phi(s)}{\partial s} ds = 0 + \int_0^1 \frac{d^2}{ds^2} \frac{\partial F}{\partial C''} \Phi(s) ds
\]

Using integration by parts twice

Factoring...

\[
\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial \varepsilon} = \frac{1}{2} \int_0^1 \left( \frac{\partial F}{\partial C} - \frac{d}{ds} \frac{\partial F}{\partial C'} + \frac{d^2}{ds^2} \frac{\partial F}{\partial C''} \right) \Phi(s) ds
\]
**Variational Solution**

The Euler Equation

\[
\frac{\partial F}{\partial C} - \frac{d}{ds} \frac{\partial F}{\partial C'} + \frac{d^2}{ds^2} \frac{\partial F}{\partial C''} = 0
\]

\[F = \alpha \left| C'(s) \right|^2 + \beta \left| C''(s) \right|^2 + 2E_{\text{ext}}(C(s))\]

\[C(s) = \{X(s), Y(s)\}\]

Separating into \(X\) and \(Y\) components:

\[2 \frac{\partial}{\partial x} E_{\text{ext}}(C(s)) - 2\alpha \frac{d^2 X(s)}{ds^2} + 2\beta \frac{d^4 X(s)}{ds^4} = 0\]

\[2 \frac{\partial}{\partial y} E_{\text{ext}}(C(s)) - 2\alpha \frac{d^2 Y(s)}{ds^2} + 2\beta \frac{d^4 Y(s)}{ds^4} = 0\]

**Method for Computing Weighting Parameter Values: Minimax Method**

Energy Surface

Solution Quality

\[E_{\text{static-true}} = \arg \max_{(\mu_{\text{true}}, \mu_{\text{det}})} (\mu_{\text{true}}, \mu_{\text{det}})\]

Pratt's FOM = \[\frac{1}{\max(N_i, N_j)} \sum_{j=1}^{N_j} \frac{1}{1 + \alpha d_{ij}^2}\]

\(N_D\): number of detected edge points

\(N_J\): number of true edge points

\(d_{ij}\): distance between \(n^{th}\) true edge point and nearest detected edge point
Gradient Vector Flow (GVF)

GVF: Generalized Gradient Vector Flow (Xu and Prince, 1998):

\[
E_{GVF}(u,v) = \frac{1}{2} \iint g(|\nabla f|)(u^2 + v^2 + 1 - g(|\nabla f|))(u - f_x)^2 + (v - f_y)^2) \, dx \, dy.
\]

\[
\begin{align*}
\frac{\partial u}{\partial \tau} &= g\nabla^2 u - (1-g)(u - f_x), \\
\frac{\partial v}{\partial \tau} &= g\nabla^2 v - (1-g)(v - f_y).
\end{align*}
\]

Minimization

\[
f(x,y) = |\nabla I(x,y)|^2, g(|\nabla f|) = \exp(-\frac{|\nabla f|}{k})
\]

GVF in snake

\[
\begin{align*}
\frac{\partial X}{\partial \tau} &= \alpha \frac{\partial^2 X}{\partial \sigma^2} - \beta \frac{\partial^3 X}{\partial \sigma^3} + u, \\
\frac{\partial Y}{\partial \tau} &= \alpha \frac{\partial^2 Y}{\partial \sigma^2} - \beta \frac{\partial^3 Y}{\partial \sigma^3} + v.
\end{align*}
\]

Generalized Gradient Vector Flow (GGVF)

We use a "force" vector, to guide the active contours in capturing the proper boundary of the leukocyte.

\[
u: \text{force in X direction}; \quad v: \text{force in Y direction}
\]

External forces \((u,v)\) are evolved from the following two Euler equations:

\[
\begin{align*}
g(|\nabla f|)\nabla^2 u - (1 - g(|\nabla f|))(u - \frac{\partial f}{\partial x}) &= 0 \\
g(|\nabla f|)\nabla^2 v - (1 - g(|\nabla f|))(v - \frac{\partial f}{\partial y}) &= 0
\end{align*}
\]

\(f\) is the gradient magnitude and \(g\) is a decreasing function ranging between \([0,1]\), e.g., a decaying exponential function.

Xu & Prince, 1998
MGVF Derivation

\[ \lim_{\alpha \to 0} \frac{E_{\text{MGVF}}(w + \alpha q) - E(w)}{\alpha} = \lim_{\alpha \to 0} \frac{1}{2\alpha} \iint \nabla w^2 \left( H(\nabla w(v', v')) + \alpha \nabla q, (v', v') \right) - H(\nabla w(v', v')) \, dx \, dy + \]

\[ \alpha \iint (H(\nabla w(v', v')) + \alpha \nabla q, (v', v')) \nabla w \nabla q \, dx \, dy + \alpha^2 \iint H(\nabla w(v', v')) \nabla q^2 \, dx \, dy + \]

\[ \left( \frac{\alpha^2}{2} \right) \iint (H(\nabla w(v', v')) + \alpha \nabla q, (v', v')) \, dx \, dy \].

Applying MVT (Mean Value Theorem):

\[ H(\nabla p(v', v')) + \alpha \nabla q, (v', v')) = \alpha \nabla q, (v', v') \frac{\partial}{\partial \alpha} H(\nabla p(v', v')) \]

where \( 0 < \theta(x, y) < 1, \forall x, y \).

\[ \lim_{\alpha \to 0} \frac{E_{\text{MGVF}}(w + \alpha q) - E(w)}{\alpha} = \frac{1}{2} \iint \left| \nabla H(\nabla w(v', v')) \nabla q, (v', v') \right| \, dx \, dy + \]

\[ \frac{1}{2} \iint (H(\nabla w(v', v')) \nabla w \nabla q) \, dx \, dy + \iint (f(w - f)q) \, dx \, dy. \]

But \( \iint \left| \nabla H(\nabla w(v', v')) \nabla q, (v', v') \right| \, dx \, dy \leq |B| \iint \nabla w^2 \nabla q, (v', v') \, dx \, dy \leq 0. \)

By Green’s theorem, \( \iint (H(\nabla w(v', v')) \nabla w \nabla q) \, dx \, dy = \int_{S_{\text{B}}} (q H(\nabla w(v', v')) \nabla w) \, d\sigma - \iint (\nabla \cdot (H(\nabla w(v', v')) \nabla w)) \, dx \, dy. \)

So, \[ \lim_{\alpha \to 0} \frac{E_{\text{MGVF}}(w + \alpha q) - E(w)}{\alpha} = \iint (f(w - f) - \nabla \cdot (H(\nabla w(v', v')) \nabla w)) \, dx \, dy. \]

Therefore, \[ \frac{\partial w}{\partial t} = -\nabla \cdot (H(\nabla w(v', v'))) \, \nabla w = \nabla (H(\nabla w(v', v')) \, \nabla w - f(w - f)). \]