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

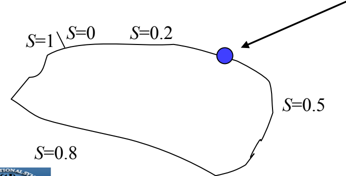
- Is the processing of dividing an image into its constituent homogeneous regions
- Example: find the closed boundary of cell

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)

Parametric Active Contour Model

$$E_{\text{snake}} = \underbrace{\frac{1}{2}\int_0^1 \left\{ \alpha \left| \frac{d\mathbf{C}(s)}{ds} \right|^2 + \beta \left| \frac{d^2\mathbf{C}(s)}{ds^2} \right|^2 \right\} ds}_{\text{Internal energy of the snake}} + \underbrace{\int_0^1 E_{\text{ext}}\big(\mathbf{C}(s)\big) ds}_{\text{External energy, computed from Image}}$$

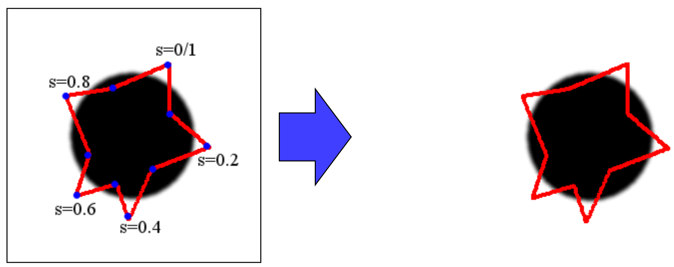


$\mathbf{C}(s) = (X(s), Y(s))$ is a snake point or snaxel and α, β are weighting parameters.

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: $E_{\text{snake}} = \frac{1}{2}\int_0^1 F(\mathbf{C}, \frac{d\mathbf{C}}{ds}, \frac{d^2\mathbf{C}}{ds^2}; s)ds$

We want: $\mathbf{C}(s)$ **that minimizes the above**

Variational Step-- Vary $\mathbf{C}(s)$ slightly: $\mathbf{C}(\varepsilon, s) = \mathbf{C}(s)+\varepsilon\,\mathbf{\Phi}(s)$.
where $\mathbf{\Phi}(0)= \mathbf{\Phi}(1)=0$

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

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

$$\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial\varepsilon} = \frac{1}{2}\int_0^1 \left(\frac{\partial F}{\partial \mathbf{C}} - \frac{d}{ds}\frac{\partial F}{\partial \mathbf{C}'} + \frac{d^2}{ds^2}\frac{\partial F}{\partial \mathbf{C}''}\right)\mathbf{\Phi}(s)ds$$

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:

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

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:

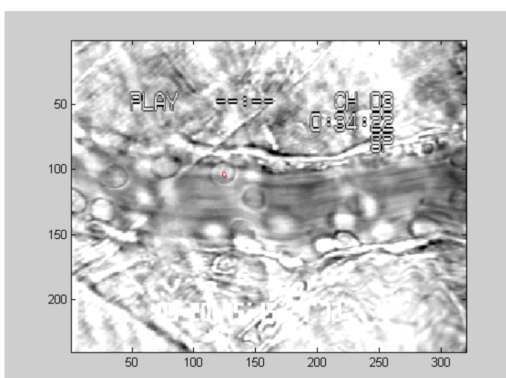
$$E_{ext}(C(s)) = -\left|\nabla\left(G_\sigma(x,y) * I(x,y)\right)\right|$$

Gradient operator Convolution

Problem: if my initial snake is away from the cell edge, the snake cant "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



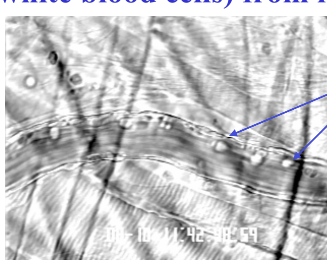
The second part of this module

- 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



Rolling leukocytes

Postcapillary venule in cremaster muscle

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**

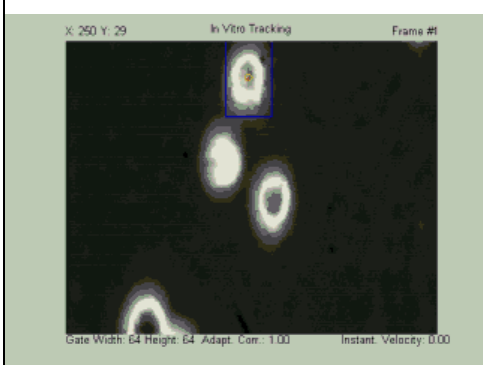
Challenges

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

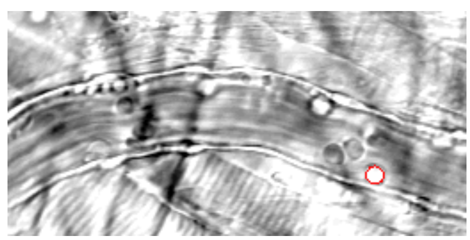
<u>We'll discuss</u>

- **Tracking**
- **Detection**

Intravital is tough!

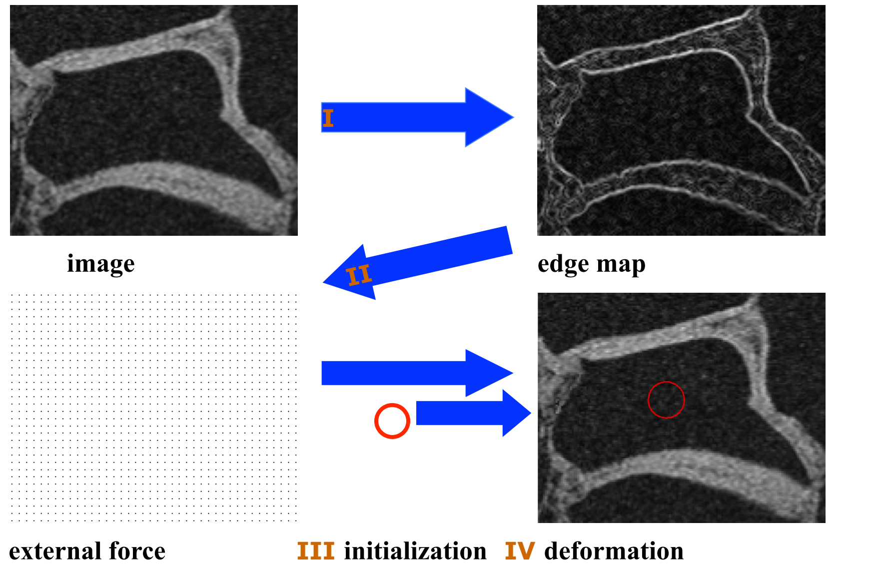


In vitro

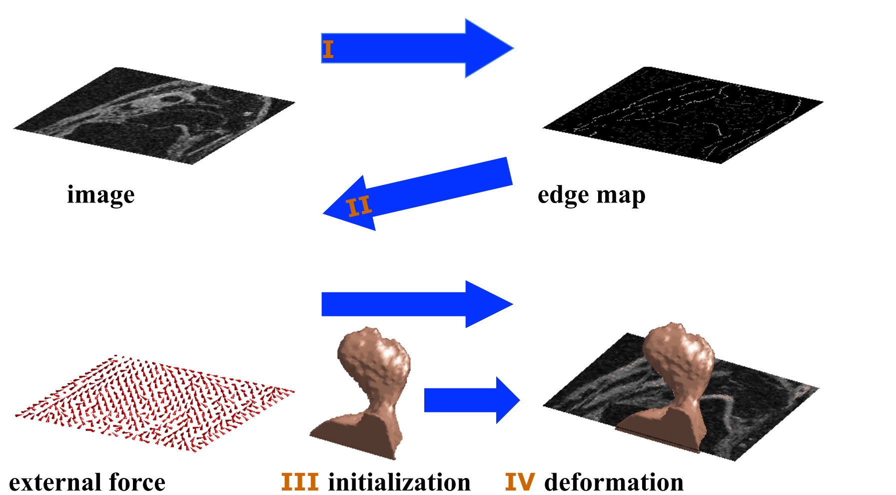


In vivo

Active Contours / Snakes



Active Surfaces



Shape-size Constrained Snake for Leukocyte Tracking

Shape-size constrained energy functional:

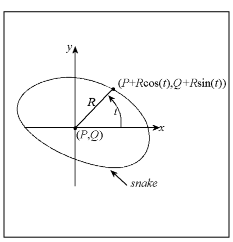
Shape

Size

Position (minimize motion orthogonal to flow)

Ray, Acton, Ley, ***Trans. Medical Imaging*****, 2002**

A Radial Snake Model for Tracking



Polar/radial snake

Proposed radial snake energy functional:

$$E_{\text{r-snake}}(P,Q,R) = E_{\text{edge}}(P,Q,R) + \mu_{\text{cons}} E_{\text{cons}}(R) + \mu_{\text{pos}} E_{\text{pos}}(P,Q,R)$$

$$E_{\text{edge}}(P,Q,R) = -\frac{1}{L_s}\int_0^{2\pi} w(P + R(t)\cos(t), Q + R(t)\sin(t))R(t)\,dt$$

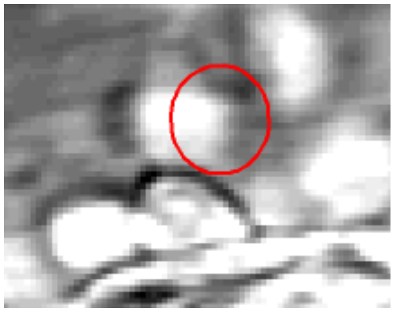
$$E_{\text{cons}}(R) = \frac{1}{2}\int_0^{2\pi} (R(t)-\rho)^2\,dt$$

$$E_{\text{pos}}(P,Q,R) = \frac{1}{2}(Q - P_Y)^2$$

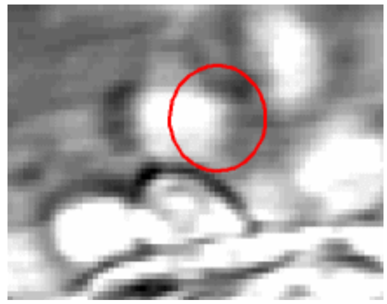
where, $L_s = \int_0^{2\pi} R(t)\,dt$

- **Fewer weights – two weights can be selected by minimax method**

Capturing Leukocyte by Shape-size Constrained Snake

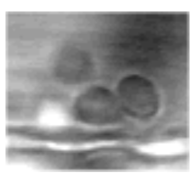


Failure of snake
without shape-size constraint

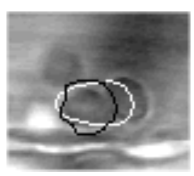


Snake successfully captures
leukocyte with shape-size constraint

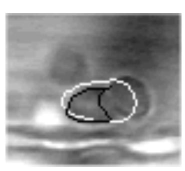
Role of shape and size constraints



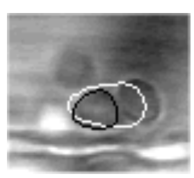
Subimage



Only shape
constraint



Only size
constraint

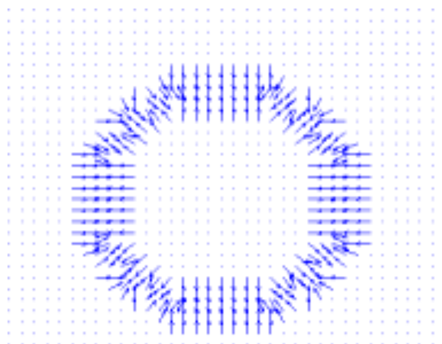


Both
constraints

White Contour – Initial **Black Contour – Final**

Gradient Vector Flow (GVF)

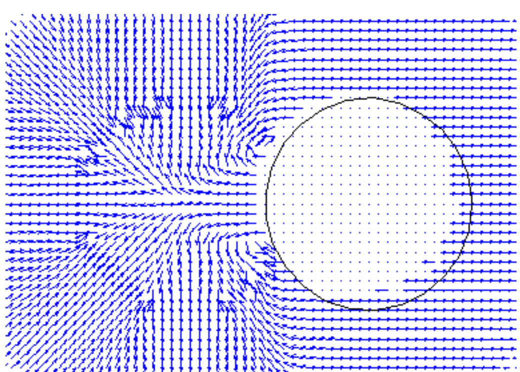
Gradient Vector Flow : Diffusion of force vectors



Xu and Prince, *IEEE Trans. Image Processing*, 1998

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)

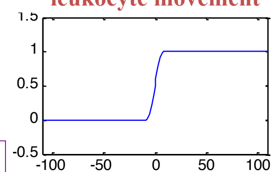
MGVF energy functional:

$$\boxed{E_{\mathrm{MGVF}}(w) = \frac{1}{2}\iint [H(\nabla w.(v^x, v^y))\,|\nabla w|^2 + f(w-f)^2]\,dxdy}$$

$f = |\nabla I|$

(v^x, v^y) : direction of leukocyte movement

Minimization



$$\boxed{\frac{\partial w}{\partial t} = \mathrm{div}(H(\nabla w.(v^x, v^y))\nabla w) - f(w-f)}$$

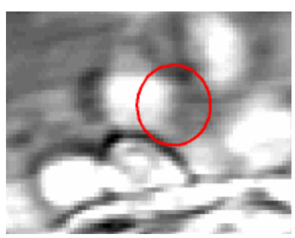
H : heaviside function

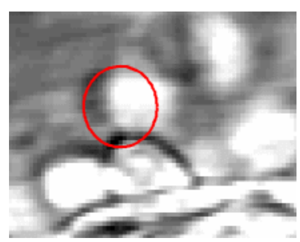
∇w : Termed as MGVF and utilized as the edge force for the snake

A *convergent* numerical implementation is derived

Ray and Acton, *IEEE Trans. Medical Imaging*, 2004

Capturing Leukocytes With MGVF





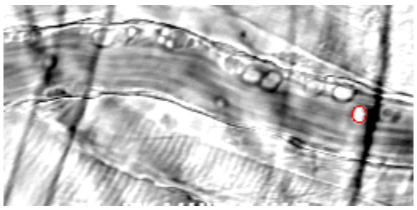
MGVF snake with cell displacement less than ρ

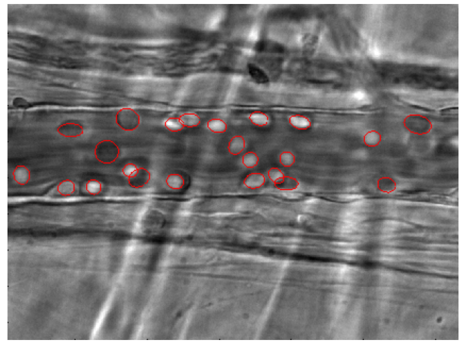
MGVF snake with cell displacement more than ρ

MGVF snake can also move backward

Direction of cell movement

Tracking Examples

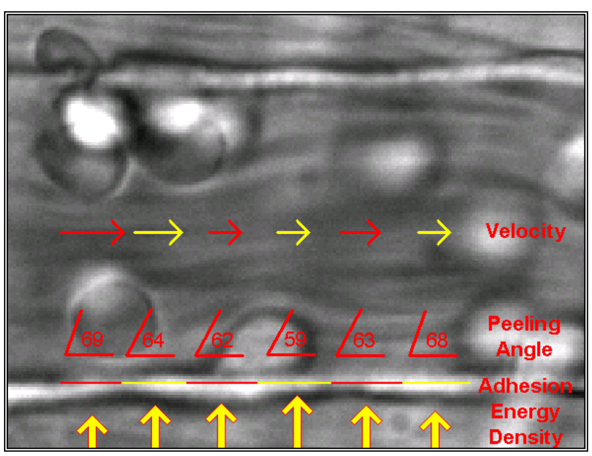




Implemented in real-time on Mercury system and NVIDIA GPU.

Can track 30 cells at 30 fps

Shape

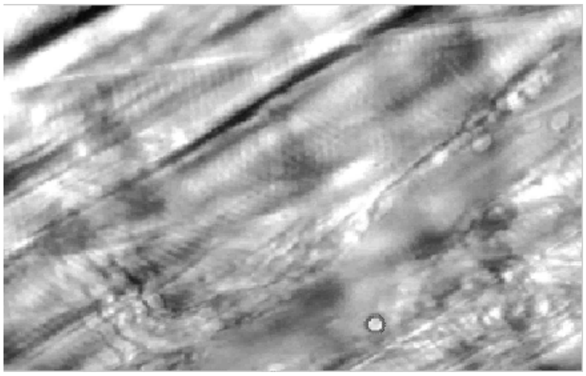


Velocity, peeling angle and adhesion energy density

Moving Field of View Tracking

Challenge:

(1) Register frames **(2) Track**

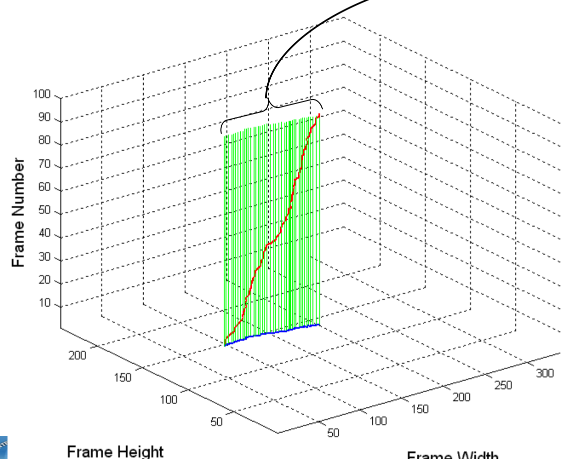


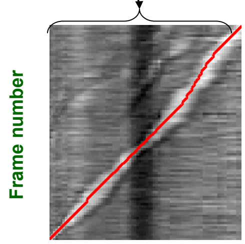
Dunne, Goobic, Acton, Ley, *Biological Procedures*, 2004

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

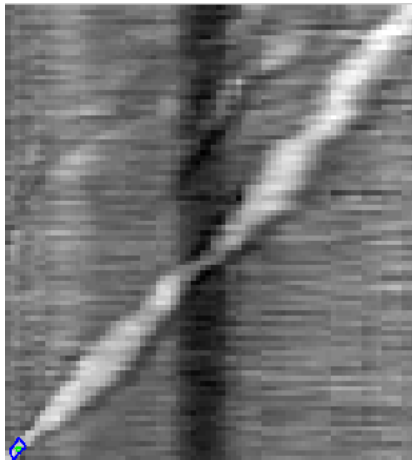




Distance along track-path

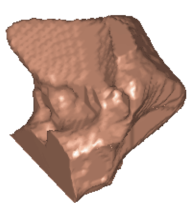
Spatiotemporal
track-path overlaid in red

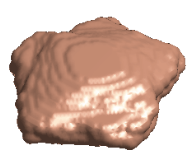
Validation example…



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





Prostate from US

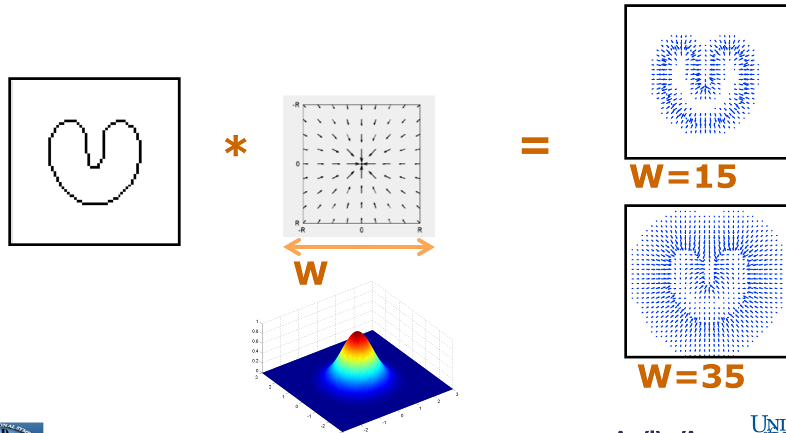
Li Acton, *IEEE Trans. IP*, 2007

Ankle from MRI

Force Generation via Vector Field Convolution (VFC)

$\boldsymbol{F}_{VFC}(x,y) = \textit{Edge Map} * \boldsymbol{K}(x,y)$

K is a prefixed vector kernel with width, ***w***



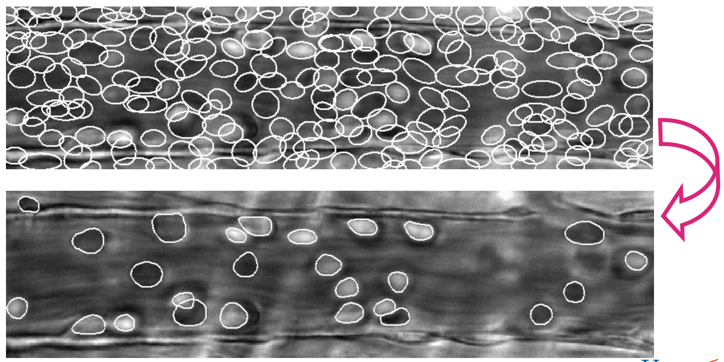
*example in AMT

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(leukocyte) > P(non-leukocyte) for a given GICOV score. A snake is used to further refine boundary.



Dong, Ray, Acton, *IEEE Trans. Med. Imaging*, 2005

The general initialization problem

- We've shown example 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?

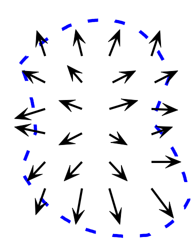
New Initialization

- 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,

$$E = \arg\min_{E} \int_{\Omega} \left\| -\nabla E - \mathbf{f} \right\|^2$$

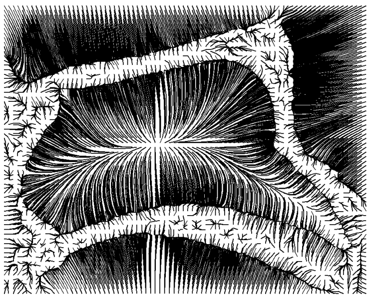


f

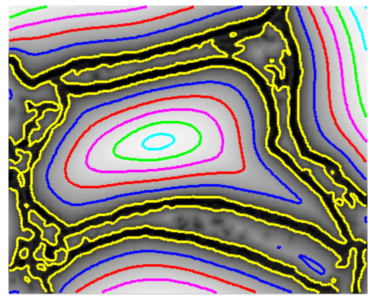
Solution – Poisson's Equation

- Poisson's equation

$$\Delta E = -\mathrm{div}\,\mathbf{f}$$



VFC field $\mathbf{f}_{vfc}$

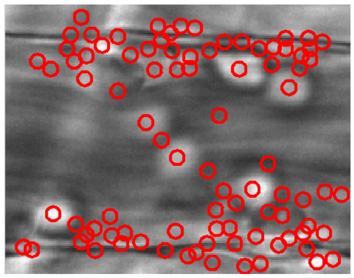


Poisson Inverse Gradient (PIG) Approach

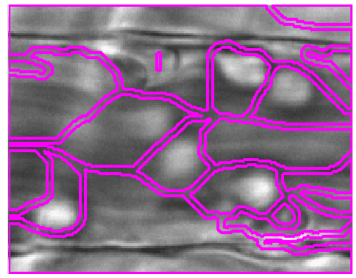
- The minimum isocontour in *E* is our initial guess
- Solution to finding *E* is given by Poisson's equation, so we call the method PIG: Poisson Inverse Gradient
- PIG
  - Accommodates broken edges / high curvature objects
  - Is Robust to noise
  - Accommodates multiple objects
  - Accelerates the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

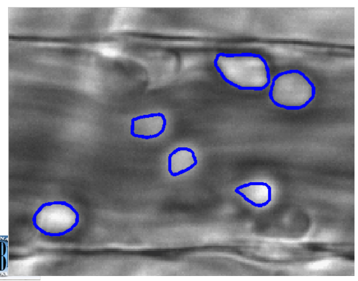
Initialization for leukocyte tracking

CoD



FFS





PIG

*examplepig in AMT

Conclusion

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

END

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:

$$-\mathbf{f}_x + \mathbf{AX} = 0$$

So the explicit method is

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

Implicit Method

The explicit method is unstable for practical time steps Δt

$$\mathbf{X}^{t+1} - \mathbf{X}^{t} = \Delta t\left(\mathbf{f}_x - \mathbf{A}\mathbf{X}^{t}\right)$$

The *implicit* method is given by

$$\mathbf{X}^{t+1} - \mathbf{X}^{t} = \Delta t\left(\mathbf{f}_x - \mathbf{A}\mathbf{X}^{t+1}\right)$$

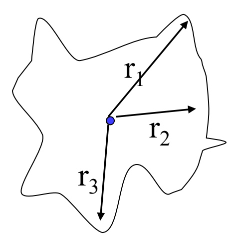
$$(\mathbf{I} + \Delta t\mathbf{A})\mathbf{X}^{t+1} = \left(\Delta t\mathbf{f}_x + \mathbf{X}^{t}\right)$$

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

Same form for Y…

Shape and Size Energy Terms

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



$$E_{\text{shape}}(\mathbf{X},\mathbf{Y}) = \frac{1}{2}\int_0^1 \left(R_x(s,X(s)) - \bar{R}(\mathbf{X},\mathbf{Y})\cos(2\pi\ s)\right)^2 ds\ + \frac{1}{2}\int_0^1 \left(R_y(s,Y(s)) - \bar{R}(\mathbf{X},\mathbf{Y})\sin(2\pi\ s)\right)^2 ds,$$

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

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

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

Variational Proof

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

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

Since limits of integration are fixed

$$= \frac{1}{2}\int_0^1 \left(\frac{\partial F}{\partial \mathbf{C}}\frac{\partial \mathbf{C}}{\partial \varepsilon} + \frac{\partial F}{\partial \mathbf{C}'}\frac{\partial \mathbf{C}'}{\partial \varepsilon} + \frac{\partial F}{\partial \mathbf{C}''}\frac{\partial \mathbf{C}''}{\partial \varepsilon}\right)ds$$ By the Chain Rule

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

Using integration by parts

$$\int_0^1 \frac{\partial F}{\partial \mathbf{C}'}\frac{\partial \mathbf{\Phi}(s)}{\partial s}ds = 0 - \int_0^1 \frac{d}{ds}\frac{\partial F}{\partial \mathbf{C}'}\mathbf{\Phi}(s)ds \qquad \int_0^1 u\,dv = uv\Big]_0^1 - \int_0^1 v\,du$$

More Variational Method

Likewise: $$\frac{\partial \mathbf{C}''(\varepsilon,s)}{\partial \varepsilon} = \frac{\partial^2 \mathbf{\Phi}(s)}{\partial s^2}$$

$$\int_0^1 \frac{\partial F}{\partial \mathbf{C}''}\frac{\partial \mathbf{C}''}{\partial \varepsilon}ds = 0 + \int_0^1 \frac{d^2}{ds^2}\frac{\partial F}{\partial \mathbf{C}''}\mathbf{\Phi}(s)ds$$ Using integration by parts twice

Factoring…

$$\frac{\partial E_{\text{snake}}(\varepsilon)}{\partial \varepsilon} = \frac{1}{2}\int_0^1 \left(\frac{\partial F}{\partial \mathbf{C}} - \frac{d}{ds}\frac{\partial F}{\partial \mathbf{C}'} + \frac{d^2}{ds^2}\frac{\partial F}{\partial \mathbf{C}''}\right)\mathbf{\Phi}(s)ds$$

Variational Solution

The Euler Equation

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

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

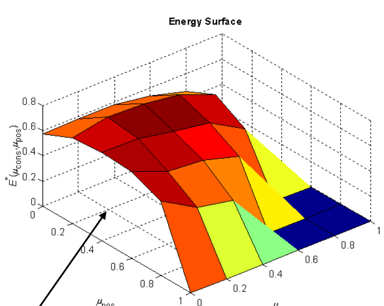
$$\mathbf{C}(s) = \{X(s), Y(s)\}$$

Separating into X and Y components:

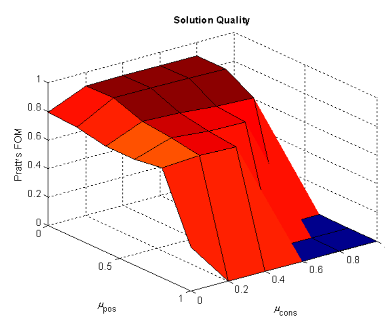
$$2\frac{\partial}{\partial x}E_{\text{ext}}(\mathbf{C}(s)) - 2\alpha\frac{d^2X(s)}{ds^2} + 2\beta\frac{d^4X(s)}{ds^4} = 0$$

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

Method for Computing Weighting Parameter Values: Minimax Method



$E^*_{\text{nonlin-rsnk}}$ *vs.* $(\mu_{\text{cons}}, \mu_{\text{pos}})$



Solution quality *vs.* $(\mu_{\text{cons}}, \mu_{\text{pos}})$

$$(\mu^*_{\text{cons}}, \mu^*_{\text{pos}}) = \underset{(\mu_{\text{cons}}, \mu_{\text{pos}})}{\arg\max}\, E^*_{\text{nonlin-rsnk}}(\mu_{\text{cons}}, \mu_{\text{pos}})$$

$$E^*_{nonlin-rsnk}(\mu_{\text{cons}}, \mu_{\text{pos}}) = \min_{P,Q,R}\{\sqrt{(1-\mu^2_{\text{cons}}-\mu^2_{\text{pos}})}(1+E_{\text{edge}}(P,Q,R)) + \mu_{\text{cons}}E_{\text{cons}}(R) + \mu_{\text{pos}}E_{\text{pos}}(P,Q,R)\}$$

$$\text{Pratt's FOM} = \frac{1}{\max(N_d, N_i)}\sum_{n=1}^{N_d}\frac{1}{1+\alpha d_n^2}$$

N_d : number of detected edge points
N_i : number of true edge points
d_n : distance between n^{th} true edge point and nearest detected edge point

Gradient Vector Flow (GVF)

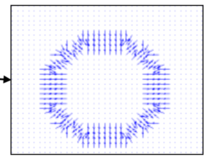
GVF: Generalized Gradient Vector Flow (Xu and Prince, 1998):

$$E_{\mathrm{GGVF}}(u,v)=\frac{1}{2}\iint[g(|\nabla f|)(u_x^2+u_y^2+v_x^2+v_y^2)+(1-g(|\nabla f|))((u-f_x)^2+(v-f_y)^2)]dxdy,$$

Minimization

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

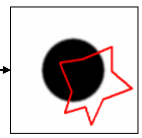
$$\frac{\partial u}{\partial \tau}=g\nabla^2 u-(1-g)(u-f_x),$$
$$\frac{\partial u}{\partial \tau}=g\nabla^2 v-(1-g)(v-f_y).$$



GVF for the circle

GVF in snake

$$\frac{\partial X}{\partial \tau}=\alpha\frac{\partial^2 X}{\partial s^2}-\beta\frac{\partial^4 X}{\partial s^2}+u,$$
$$\frac{\partial Y}{\partial \tau}=\alpha\frac{\partial^2 Y}{\partial s^2}-\beta\frac{\partial^4 Y}{\partial s^2}+v.$$



A circle and GVF snake evolution

Generalized Gradient Vector Flow (GGVF)

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

u: force in X direction; *v*: force in Y direction

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

$$g(|\nabla f|)\nabla^2 u-(1-g(|\nabla f|))(u-\frac{\partial f}{\partial x})=0$$
$$g(|\nabla f|)\nabla^2 v-(1-g(|\nabla f|))(v-\frac{\partial f}{\partial y})=0$$

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

$$\lim_{\alpha\to 0}\frac{E_{\mathrm{MGVF}}(w+\alpha q)-E(w)}{\alpha}=\lim_{\alpha\to 0}[\frac{1}{2\alpha}\iint|\nabla w|^2\,(H(\nabla w.(v^x,v^y)+\alpha\nabla q.(v^x,v^y))-H(\nabla w.(v^x,v^y)))dxdy+$$

$$\alpha\iint(H(\nabla w.(v^x,v^y)+\alpha\nabla q.(v^x,v^y))\nabla w.\nabla q)dxdy+\frac{\alpha^2}{2}\iint(H(\nabla w.(v^x,v^y)+\alpha\nabla q.(v^x,v^y))\left|\nabla q\right|^2)dxdy+$$

$$\alpha\iint(f(w-f)q)dxdy+\frac{\alpha^2}{2}\iint f\alpha^2q^2dxdy].$$

Applying MVT (Mean Value Theorem):

$$H(\nabla p.(v^x,v^y)+\alpha\nabla q.(v^x,v^y))-H(\nabla p.(v^x,v^y))=\alpha\nabla q.(v^x,v^y)H'(\nabla p.(v^x,v^y)+\alpha\theta\nabla q.(v^x,v^y)),$$

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

$$\lim_{\alpha\to 0}\frac{E_{\mathrm{MGVF}}(w+\alpha q)-E(w)}{\alpha}=\frac{1}{2}\iint(\left|\nabla w\right|^2H'(\nabla w.(v^x,v^y))\nabla q.(v^x,v^y))dxdy+$$

$$\lambda\iint(H(\nabla w.(v^x,v^y))\nabla w.\nabla q)dxdy+\iint(f(w-f)q)dxdy,$$

But, $\left|\iint(\left|\nabla w\right|^2H'(\nabla w.(v^x,v^y))\nabla q.(v^x,v^y))dxdy\right|\le B\left|\iint_{S=\{(x,y):|\nabla w.(v^x,v^y)|\le\varepsilon\}}|\nabla w|^2\,\nabla q.(v^x,v^y)dxdy\right|\approx 0.$

By Green's theorem, $\iint(H(\nabla w.(v^x,v^y))\nabla w.\nabla q)dxdy=\int_{\partial\Omega}(qH(\nabla w.(v^x,v^y))\nabla w)d\sigma-\iint(q\operatorname{div}(H(\nabla w.(v^x,v^y))\nabla w))dxdy.$

So, $\lim_{\alpha\to 0}\frac{E_{\mathrm{MGVF}}(w+\alpha q)-E(w)}{\alpha}=\iint((f(w-f)-\operatorname{div}(H(\nabla w.(v^x,v^y))\nabla w))q)dxdy.$

Therefore, $\boxed{\frac{\partial w}{\partial\tau}=-\frac{\delta E_{MGVF}}{\delta w}=\operatorname{div}(H(\nabla w.(v^x,v^y))\nabla w)-f(w-f).}$