Introduction to Some Medical Imaging Problems and Related TV Techniques

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- Perfusion Kernel Estimation
- Phase Unwrapping
- Image Registration

⋆ Vascular Reconstruction and Identification

Perfusion Kernel Estimation

- Perfusion modeled by:

$$C_{\mathrm{VOI}}(t) = F \int_0^t C_{\mathrm{a}}(\tau) R(t-\tau) d\tau$$

where:

$C_{\mathrm{VOI}}(t)$: concentration of tracer still present in volume of interest (VOI) after time t.

$C_{\mathrm{a}}(t)$: concentration of tracer injected at time t on arterial side of VOI.

F: tissue flow rate.

$R(t)$: fraction of injected tracer still present in VOI after time t.

- $F \cdot R(t)$ quantifies tissue perfusion...
- Goal: Estimate perfusion kernel, $F \cdot R(t)$, from known/measured $C_{\mathrm{a}}(t)$ and $C_{\mathrm{VOI}}(t)$ measured from images.

Methods:

- Model $F \cdot R(t)$ with branching capillaries.
  Estimate few model parameters.
- Regularized singular value decomposition.
- Fourier filtering.
- Penalize increasing $F \cdot R(t)$.

Note: $R(t)$ (fraction left) is *non-increasing*.

Proposed Approach:

- Set up natural discretization:

  $F \int_0^t C_\mathrm{a}(\tau) R(t-\tau) d\tau = C_\mathrm{VOI}(t) \to A\boldsymbol{b} = \boldsymbol{c}$

- Solve in some best fit manner:

$$\min_b \|A\boldsymbol{b} - \boldsymbol{c}\|$$

- Subject to non-increasing R:

$$D\boldsymbol{b} \geq 0.$$

Some Questions:

- What kind of discretization?
  - Smooth splines make functions look nice and perhaps more realistic.
  - Solution constrained to be non-increasing means bounded in BV. $BV \xrightarrow{c} L^p$ means convergence guaranteed in L^p.
- What norm to minimize?
  - Quadratic program solver for:

$$\min_{\boldsymbol{b}} \|A\boldsymbol{b} - \boldsymbol{c}\|_{\ell_2}^2 \text{ s.t. } D\boldsymbol{b} \geq 0.$$

  - Simplex or interior point methods for:

$$\min_{\boldsymbol{b}} \|A\boldsymbol{b} - \boldsymbol{c}\|_{\ell_1} \text{ s.t. } D\boldsymbol{b} \geq 0.$$

  - ℓ_1 measure more statistically robust.
  - ℓ_1 measure leads to non-uniqueness and sometimes "jagged" solutions.

On TV, BV

- Familiar 1D formulation of TV:

$$TV(f) = \sup_{\{x_i\}} \sum_i |f(x_{i+1}) - f(x_i)|$$

e.g., $TV(cs(x)) = c$, $TV(\sin(1/x)) = \infty$.

- In general:

$$\int_\Omega |\nabla f| \sim \sup_{|\boldsymbol{\psi}|\le 1} \int_\Omega \nabla f \cdot \boldsymbol{\psi} \sim \sup_{|\boldsymbol{\psi}|\le 1} \int_\Omega f \nabla \cdot \boldsymbol{\psi}$$

So,

$$TV_\Omega(f) = \sup_{\boldsymbol{\psi}\in\mathcal{C}(\Omega)} \int_\Omega f \nabla \cdot \boldsymbol{\psi}$$

where:

$$\mathcal{C}(\Omega) = \{\boldsymbol{\psi} \in C_0^1(\Omega, \boldsymbol{R}^n) : |\boldsymbol{\psi}| \le 1\}$$

e.g.,

$$TV_{\boldsymbol{R}^n}(c\chi_B) = c \cdot \text{perim}(B),$$

$$TV_Q(\chi_1 + \chi_2) = \text{jump} \cdot \text{edge\_length}$$

- Function spaces: $W^{1,1}(\Omega) \subset BV(\Omega)$

$$\|f\|_{BV(\Omega)} = \|f\|_{L^1(\Omega)} + TV_\Omega(f)$$

$$\|f\|_{W^{1,1}(\Omega)} = \|f\|_{L^1(\Omega)} + \|\nabla f\|_{L^1(\Omega,\boldsymbol{R}^n)}$$

but <u>BV allows jumps</u>.

On Statistical Robustness of ℓ_1, L^1

- Reduction to simple example:

$$\min_C \|C - X\| \ \ldots \ \min_c \|c\boldsymbol{e} - \boldsymbol{x}\|$$

$$\boldsymbol{e} = \langle 1, 1, \ldots, 1 \rangle \in \boldsymbol{R}^{n+1}$$

$$\boldsymbol{x} \approx \langle a, b, b, \ldots, b \rangle, \quad a > b > 0.$$

- Use ℓ_1:

$$\min_c \|c\boldsymbol{e} - \boldsymbol{x}\|_{\ell_1} = \min_c \sum_i |c - x_i|$$

$$= \min_{a \le c \le b} [(a - c) + n(c - b)]$$

$$\ldots c^* = b.$$

Outlier a ignored.

- Use ℓ_2:

$$\min_c \|c\boldsymbol{e} - \boldsymbol{x}\|_{\ell_2}^2 = \min_c \sum_i (c - x_i)^2$$

$$= \min_{a \le c \le b} [(a - c)^2 + n(c - b)^2]$$

$$\ldots c^* = \frac{a + nb}{1 + n}.$$

Outlier a pulls solution toward it.

On Non-uniqueness of ℓ_1, L^1

- Reduction to simple example:

$$\min_u \{\|u - f\|_{L^1} + \mu TV(u)\} \ldots$$

$$\min_{u_1, u_2} \{|u_1 - f_1| + |u_2 - f_2| + |u_2 - u_1|\}$$

$$f_2 > f_1$$

- μ small $\Rightarrow u_i = f_i \Rightarrow$

$$\min = \mu |f_2 - f_1|.$$

- μ large $\Rightarrow u_1 = u_2 = \bar{u} \Rightarrow$

$$\min = |\bar{u} - f_1| + |\bar{u} - f_2|$$

$$f_1 \le \bar{u} \le f_2?$$

- $f(x) = \Sigma\, f_i \chi_i(x) \approx x$:

u can have a jagged staircase look.
Jagged or not gives same TV.

Phase Unwrapping

- Raw image data: complex, noisy $\tilde{\rho}$,

$$\tilde{\rho} = \Re\{\tilde{\rho}\} + \hat{i}\Im\{\tilde{\rho}\} = r\exp(\hat{i}\phi)$$

  - magnitude r: intensity, absorption
  - phase ϕ: velocity, temperature

- Wrapped phase:

$$\phi = \tan^{-1}(\Im\{\tilde{\rho}\}/\Re\{\tilde{\rho}\}) \in (-\pi, \pi]$$

- Wrapped phase contains:
  - noise,
  - artificial jumps from wrapping,
  - genuine jumps from real boundaries.

- Goal: Estimate true phase, free from noise and artificial jumps. Example.

- Not a recent problem, various methods, none completely satisfying.

- Proposed Approach: Minimize

$$J(r,\phi) = \frac{1}{2}\|\tilde{\rho} - re^{\hat{i}\phi}\|^2_{L^2(P)} + \mu_1 TV_P(r) + \mu_2 TV_P(\phi)$$

• Formally,

$$J(r,\phi) = \frac{1}{2}\int_P |\Re\{\tilde{\rho}\} - r\cos(\phi)|^2$$

$$+\frac{1}{2}\int_P |\Im\{\tilde{\rho}\} - r\sin(\phi)|^2$$

$$+\mu_1\int_P |\nabla r| + \mu_2\int_P |\nabla\phi|$$

• Optimality conditions:

$$\begin{cases} \Re\{\tilde{\rho}\}\cos(\phi) + \Im\{\tilde{\rho}\}\sin(\phi) \\ \qquad -r + \mu_1\nabla\cdot\left(\dfrac{\nabla r}{|\nabla r|}\right) = 0, \ P \\ \Im\{\tilde{\rho}\}r\cos(\phi) - \Re\{\tilde{\rho}\}r\sin(\phi) \\ \qquad +\mu_2\nabla\cdot\left(\dfrac{\nabla\phi}{|\nabla\phi|}\right) = 0, \ P \\ \mu_1\dfrac{\partial r}{\partial n} = \mu_2\dfrac{\partial\phi}{\partial n} = 0, \ \partial P \end{cases}$$

• Consider numerical method for, say,

$$F(u) + \mu\nabla\cdot(G(|\nabla u|)\nabla u) = 0$$

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- Discretize:

$$u_t = F(u) + \mu\nabla \cdot (G(|\nabla u|)\nabla u)$$

  semi-implicitly:

$$\frac{u^{n+1} - u^n}{\Delta t} = F(u^n) + \mu\nabla \cdot (G(|\nabla u^n|)\nabla u^{n+1})$$

- So use outer iteration:

$$u^{n+1} - \mu\Delta t\nabla \cdot (G^n \nabla u^{n+1}) = u^n + \Delta t F^n$$

  and, say, Jacobi inner iteration.

- $G^n = G(|\nabla u^n|)$ can require careful treatment for TV-stable scheme.

- With $F(u) = \tilde{u} - u$, $\Delta t = 1$, we get Picard iteration:

$$u^{n+1} - \mu\nabla \cdot (G^n \nabla u^{n+1}) = \tilde{u}.$$

- Newton iteration can have indefinite Jacobian.

Image Registration

- Goal: Identify the coordinate transformation between two images which connects tissue sites in one to their corresponding location in the other.
- Two images can be from:
  - Same patient, different times,
  - Same patient, different modalities,
  - Two different patients,
  - A patient and an idealized atlas.
- Examples:
  - Establishing norms among patients,
  - Intraoperative registration between MRI and CT images for image-guided surgery,
  - Mammogram sequences to determine tracer uptake by tumors.
- Types of transformations:
  - Rigid. Not completely trivial, but easier and useful in some cases.
  - Non-rigid. The current challenge.

The Current Favorite:

- Form of transformation:

$$T = T_{\text{global}} + T_{\text{local}}$$

where:

$$T_{\text{global}} \sim \text{linear}, \quad T_{\text{local}} \sim \text{splines}$$

- Given images, I_0 and I_1, minimize:

$$J(T) = S(I_1, I_0(T)) + \mu \int_P (D^2 T)^2$$

where $S(I_1, I_2)$ measures mutual information between I_1 and I_2...

- If $I_1 = v_1$ in many pixels where $I_2 = v_2$, then $S(I_1, I_2)$ is smaller.
- If I_2 assumes many values in pixels where $I_1 = v_1$, then $S(I_1, I_2)$ is larger.
- $S(I_1, I_2)$ has explicit formulation in terms of frequencies (probabilities) of pixel values occurring together.

- Proposed Approach: Use variational principle which determines the registration transformation as the one which is *as rigid as possible*.
- For example,
  1. Construct transition images, $\{I(x,y;z) : (x,y) \in P, 0 \le z \le 1\}$ by:
  $$\min_I \Big\{ \int_P |I - I_0|_{z=0} + \int_P |I - I_0|_{z=1} + \int_{P\times[0,1]} |\nabla I| \Big\}$$
  2. Use result to construct convection field (optical flow) by:
  $$\min_{(u,v)} \int_{P\times[0,1]} \Big[|uI_x + vI_y + I_z| + |\nabla u| + |\nabla v| \Big]$$
  3. Integrate convection field to obtain transformation:
  $$\frac{dx}{dz} = u(x,y,z), \quad \frac{dy}{dz} = v(x,y,z)$$
- Works for simple examples.
- Compress to single variational problem.

Vascular Reconstruction and Identification

New Technology: New blood pooling contrast agents provide stunning images.
(See pictures.)

Goals:

- Segment 3D image into points inside vessels and points outside vessels.
  - Simple thresholding not enough,
  - Background variation (RF inhomogeneity) frustrates process.
- Facilitate visualization:
  - 3D-shaded rendering,
  - Maximum intensity projection,
  - Highlight arteries and veins separately,
  - Reveal shunts, stenoses, aneurisms, etc.
- Facilitate measurement:
  - Vessel diameter,
  - Plaque depth.
- Perform virtual angiography.

- Proposed approach to reconstruct image:

$$\min_{I,M}\left\{ \int_Q |I - M\hat{I}|^2 + 2\mu \int_Q F(|\nabla I|) \right.$$

$$\left. +\lambda_1 \int_Q |\nabla M|^2 + \lambda_2 \int_Q |\Delta M|^2 \right\}$$

- $\hat{I}$ is raw image.
- M is multiplier field to remove background variation from $\hat{I}$.
- F is chosen to sharpen I and to penalize background variation in I. (More later.)
- Optimality conditions:

$$\begin{cases} -(I - M\hat{I}) + \mu\nabla\cdot(G(|\nabla I|)\nabla I) = 0, & Q \\ (I - M\hat{I})\hat{I} + \lambda_1\Delta M - \lambda_2\Delta^2 M = 0, & Q \\ \dfrac{\partial I}{\partial n} = \dfrac{\partial M}{\partial n} = \Delta M = \dfrac{\partial \Delta M}{\partial n} = 0, & \partial Q \end{cases}$$

where $G(t) = F'(t)/t$.

- Numerical solution by Picard iteration.

- Given I reconstructed from $\hat{I}$, how to perform segmentation?
- Proposed approach: Use region growing procedure based on levels sets:

$$\begin{cases} \ell_t = g|\nabla \ell|[\nu + \kappa] \\ \\ \ell(\boldsymbol{x}, 0) = \pm \mathrm{dist}(\boldsymbol{x}, S), \quad S \text{ in vessel} \end{cases}$$

$$g = \frac{1}{1 + |\nabla I|}, \quad \kappa = \nabla \cdot \left(\frac{\nabla \ell}{|\nabla \ell|} \right)$$

- Same tool for virtual angiography: restrict growth to flow direction.

On Level Set Methods

- Instead of:

$$\frac{\boldsymbol{x}(t,p)}{dt} = s\hat{\boldsymbol{n}}, \qquad s = \text{normal speed}$$

take:

$$\ell(\boldsymbol{x}(t),t) = c \longrightarrow \ell_t + \nabla\ell \cdot \boldsymbol{x}' = 0$$

or:

$$0 = \ell_t + |\nabla\ell|\frac{\nabla\ell}{|\nabla\ell|} \cdot \boldsymbol{x}' = \ell_t + |\nabla\ell|s$$

- Suppose

$$\begin{cases} \ell_t &= g|\nabla\ell|, \qquad g = \dfrac{1}{1+|\nabla I|} \\ \ell(\boldsymbol{x},0) &= \pm\text{dist}(\boldsymbol{x},S), \quad S \text{ in vessel} \end{cases}$$

Then ℓ loses regularity rapidly and fails objective. (See picture.)

- Appropriate dissipation: (See picture.)

$$\ell_t = g|\nabla\ell|[\nu+\kappa], \quad \kappa = \nabla \cdot (\nabla\ell/|\nabla\ell|)$$

  - If $\ell = c$ on opposite (same) side of tangent as $\nabla\ell$, then $\kappa > 0$ ($\kappa < 0$).
  - Where $\ell = c$ convex, $\kappa < 0$ decelerates front; else, $\kappa > 0$ accelerates front.

- Proposed approach for separating arteries and veins:
  - Identify all diverging tree structures.
  - Let expert user decide which tree structures are arterial or venous.
- Procedure for identifying diverging tree structures:
  - Use region growth,

    $$\ell_t = g|\nabla \ell|[\nu + \kappa]S(\kappa + \tau)$$

    where:

    $$S(\kappa) = \begin{cases} 1, & \kappa \geq 0 \\ 0, & \kappa < 0 \end{cases}$$

    and $1/\tau$ is minimum radius permitted at convex portions of vessel boundary.
  - Seed growth in largest vascular regions and set $1/\tau$ correspondingly large.
  - Increase τ until diverging structures are complete or until they meet at shunts.

Current Detailed Investigation

- Choosing best F for image enhancement:

$$\min_I \left\{ \frac{1}{2} \int_P |I - \tilde{I}|^2 + \mu \int_P F(|\nabla I|) \right\}$$

- Optimality system:

$$(I - \tilde{I}) - \mu \nabla \cdot (G(|\nabla I|) \nabla I) = 0$$

  where $G(t) = F'(t)/t$.

- After some calculations,

$$\frac{1}{\mu}(\tilde{I} - I) +$$

$$G(|\nabla I|) I_{\tau\tau} + F''(|\nabla I|) I_{nn} = 0$$

  where:

  τ tangential to level sets,
  n normal to level sets.

- Can now make shopping list for enhancement...

$$\frac{1}{\mu}(\tilde{I} - I) + G(|\nabla I|)I_{\tau\tau} + F''(|\nabla I|)I_{nn} = 0$$

- Edge: As $|\nabla I| \to \infty$, $\dfrac{F''}{G} \to 0$.

  e.g., TV penalty,

  $$F(t) = t,\ G(t) = \frac{1}{t},\ F''(t) = 0,\ \frac{F''}{G} = 0.$$

- Grey: For $\delta \le |\nabla I| \le B$, $\dfrac{F''}{G} = \mathcal{O}(1)$.

  e.g., with $a \sim 1/B^2$,

  $$F(t) = \tfrac{1}{2a}\log(1 + at^2),\ G(t) = \frac{1}{1 + at^2},$$

  $$F''(t) = \frac{1 - at^2}{(1 + at^2)^2},\ \frac{F''}{G} = \frac{1 - at^2}{1 + at^2}.$$

- Flat: As $|\nabla I| \to 0$, $G(t) = \dfrac{F'(t)}{t} \to F''(0)$.

  $$GI_{\tau\tau} + F''I_{nn} \to F''(0)\Delta I,\ F''(0) \text{ large}.$$

  e.g., Gaussian penalty,

  $$F(t) = bt^2,\ G(t) = 2b,\ F''(t) = 2b,$$

  and $GI_{\tau\tau} + F''I_{nn} = 2b\Delta I$.

$$\frac{1}{\mu}(\tilde{I} - I) + G(|\nabla I|)I_{\tau\tau} + F''(|\nabla I|)I_{nn} = 0$$

- Shopping list for sharpening...same as before but,
- Grey: For $\delta \leq |\nabla I| \leq B$, $\dfrac{F''}{G} = \mathcal{O}(1)$

  and $F'' < 0$.

  e.g., with $a \sim 1/\delta^2$,

  $$F(t) = \tfrac{1}{2a}\log(1 + at^2),\ G(t) = \frac{1}{1 + at^2},$$

  $$F''(t) = \frac{1 - at^2}{(1 + at^2)^2},\ \frac{F''}{G} = \frac{1 - at^2}{1 + at^2}.$$
- However, consider:

  $$\begin{cases} u_t = (g(u_x)u_x)_x, & g(v) = \dfrac{1}{1 + av^2} \\ u(0) = 1 + \tanh(x) \end{cases}$$

  - It is not enough that $F'' < 0$. (See pictures.)
  - Not always sharpened to desired step.