Detection and segmentation of cell nuclei

Al-Kofahi et al., IEEE TBME 2010

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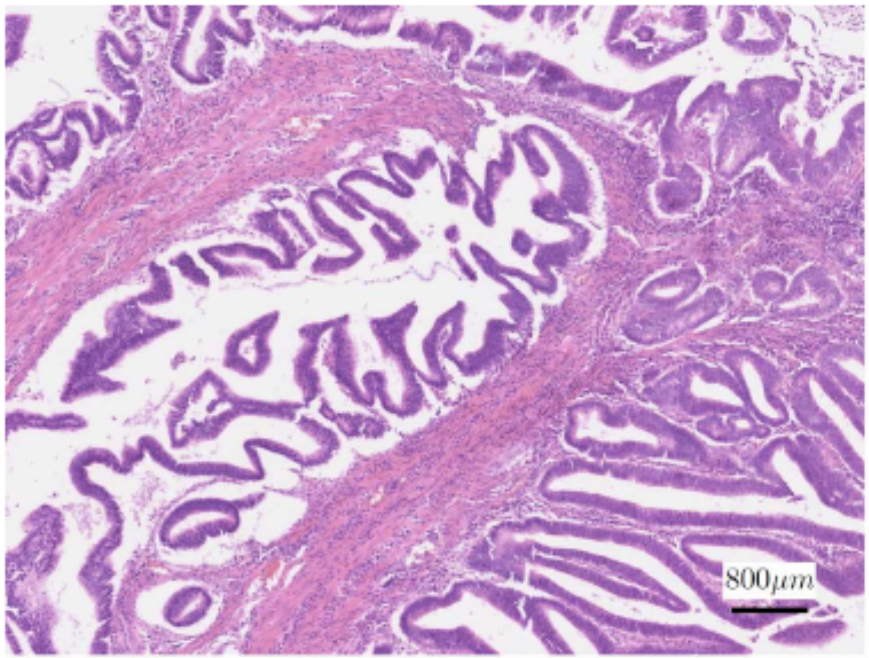
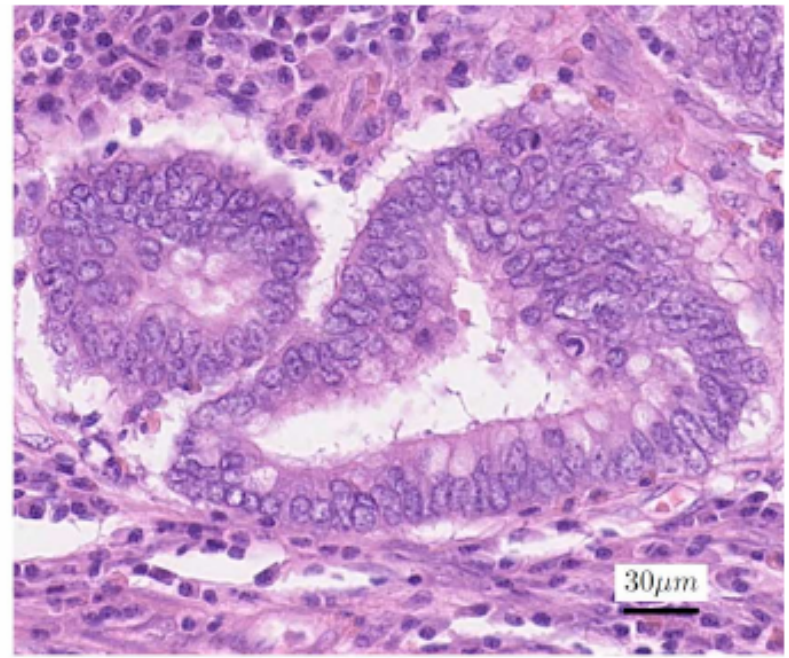
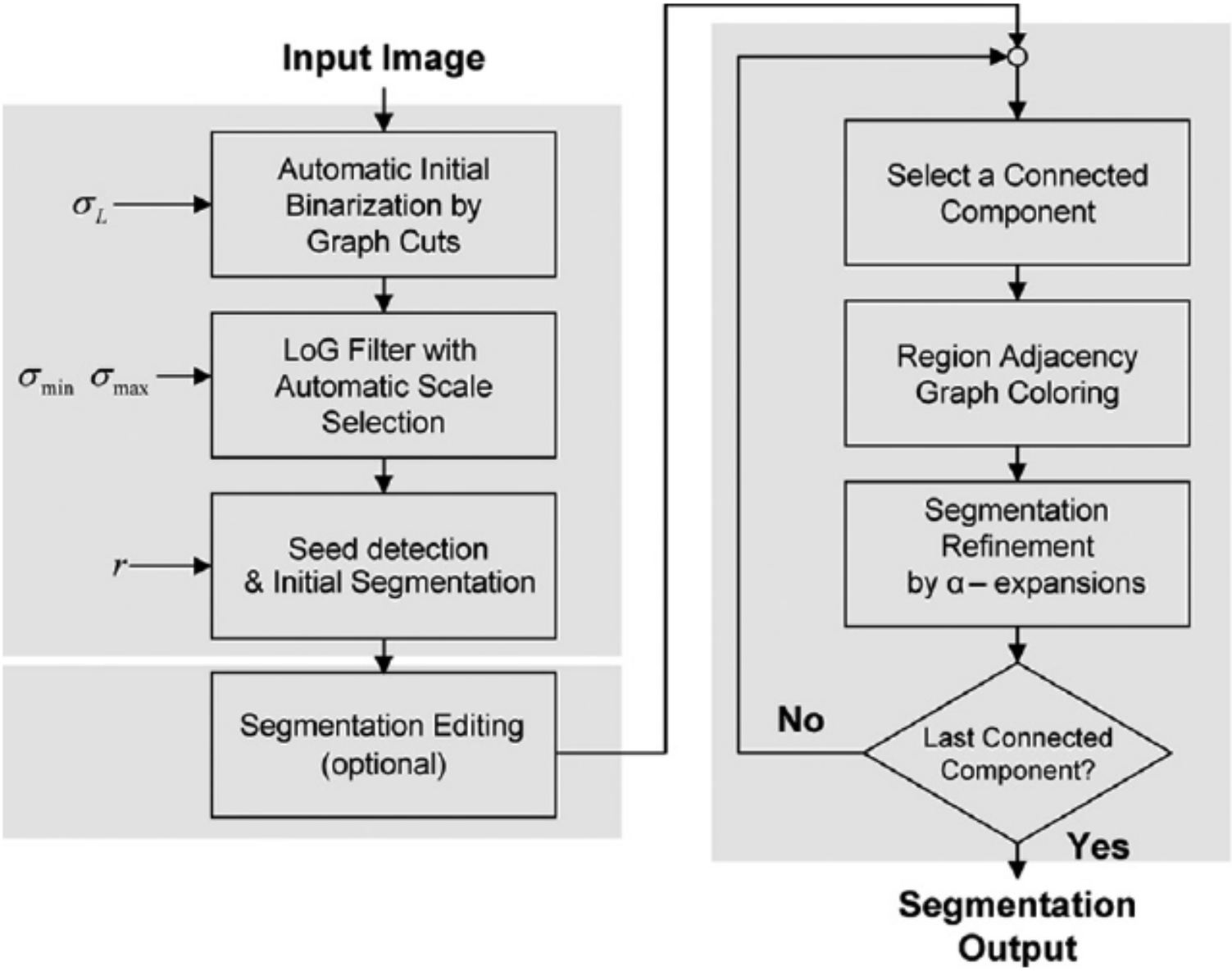
Histology images





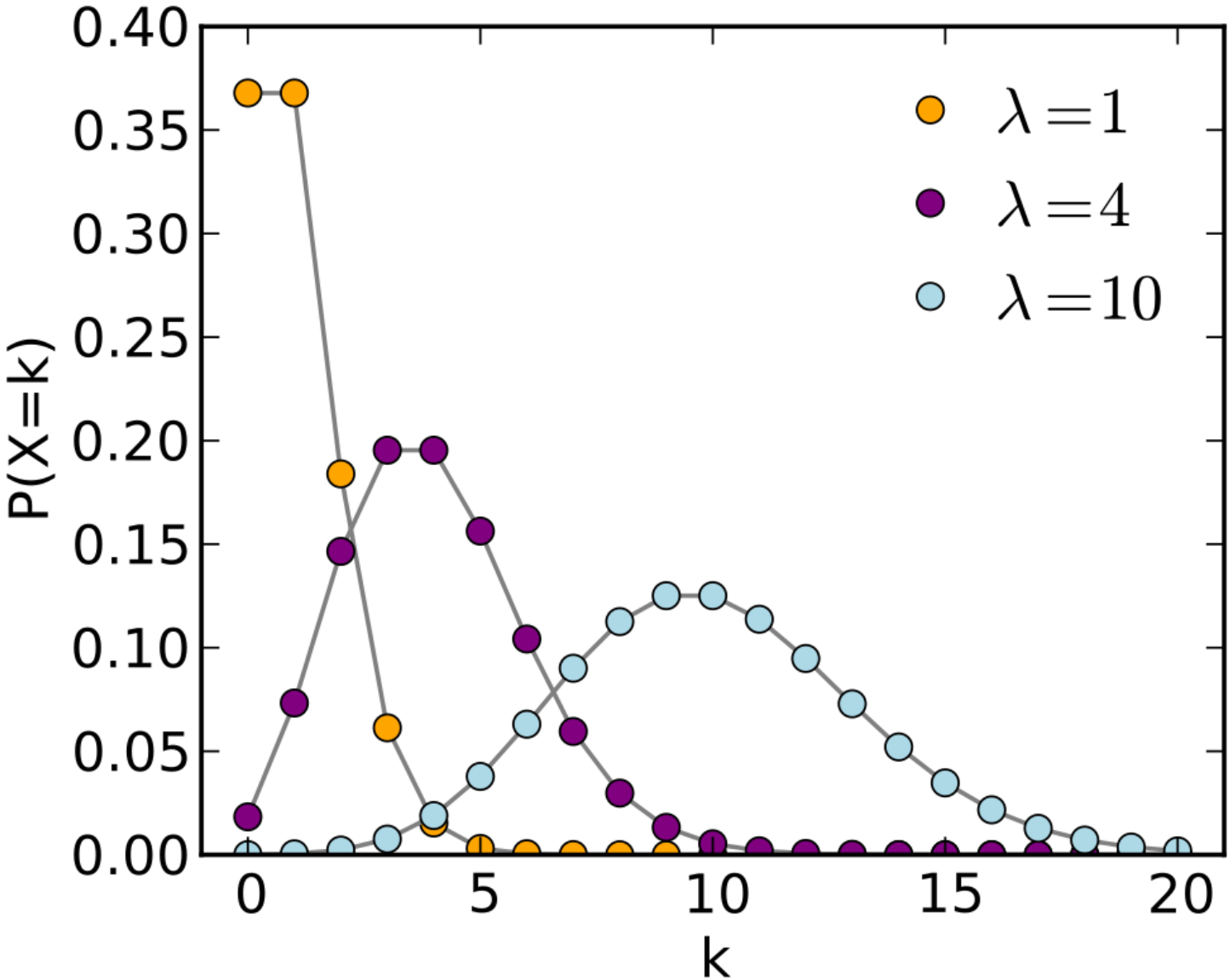
- Hematoxylin (nuclei, blue) & eosin (extracellular matrix and cytoplasm, pink)
- **Task:** find and segment cell nuclei $\rightarrow$ counting cells, diagnostics

Method


Input Image
σ_L
Automatic Initial Binarization by Graph Cuts
σ_{min} σ_{max}
LoG Filter with Automatic Scale Selection
r
Seed detection & Initial Segmentation
Segmentation Editing (optional)
Select a Connected Component
Region Adjacency Graph Coloring
Segmentation Refinement by α – expansions
No
Last Connected Component?
Yes
Segmentation Output

Poisson distribution

- $p(k) = \frac{\lambda^k e^{-\lambda}}{k!}$



Binarization - Poisson modeling

- Calculate histogram
- Model as a Poisson mixture ($\mu = \lambda$)

$$h(i) = P_0 \times p(i|0) + P_1 \times p(i|1)$$

- find threshold t minimizing KL divergence between model and histogram

$$t^* = \arg\min_t \{\mu - P_0(t)(\ln P_0(t) + \mu_0(t) \ln \mu_0(t)) - P_1(t)(\ln P_1(t) + \mu_1(t) \ln \mu_1(t))\}$$

$$P_0(t) = \sum_{i=0}^{t} h(i), \qquad \mu_0(t) = \frac{1}{P_0(t)} \sum_{i=0}^{t} i \times h(i)$$

$$P_1(t) = \sum_{i=t+1}^{I_{max}} h(i), \qquad \mu_1(t) = \frac{1}{P_1(t)} \sum_{i=t+1}^{I_{max}} i \times h(i).$$

Binarization Graphcuts

$$E(L(x,y)) = \sum_{(x,y)} D(L(x,y); I_N(x,y)) + \sum_{(x,y)} \sum_{(x',y') \in N(x,y)} V(L(x,y), L(x',y'))$$

- maximum log likelihood unary term

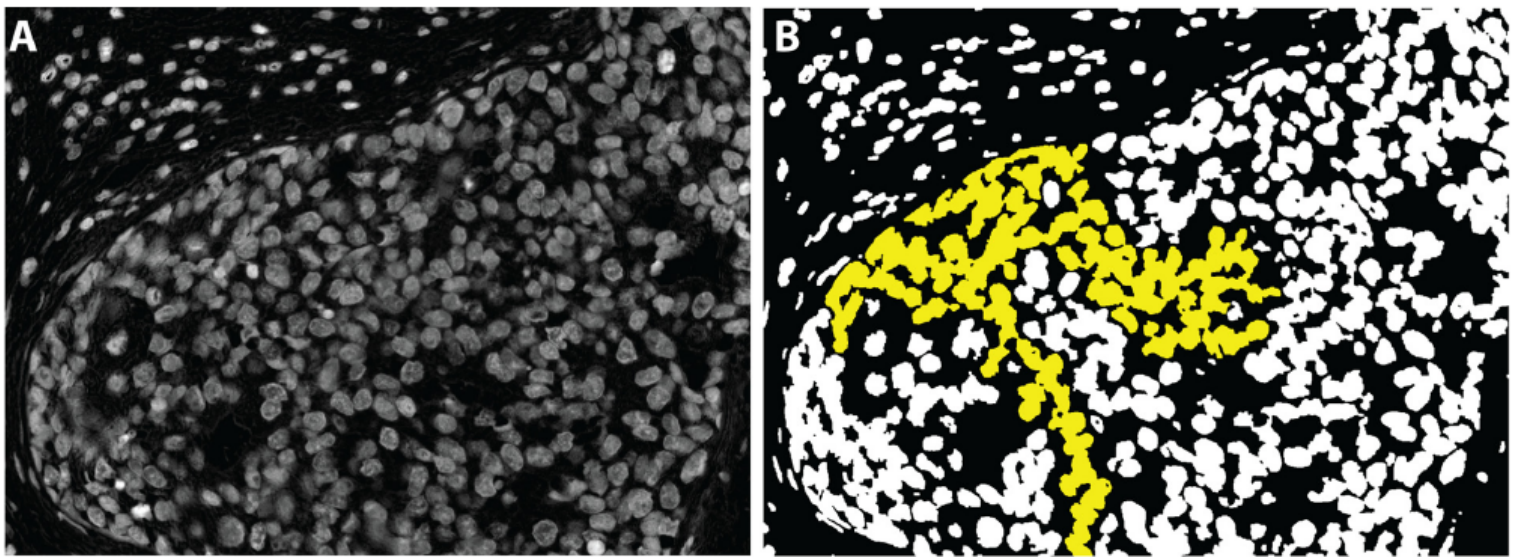
$$D(L(x,y);\, I_N(x,y)) = -\ln p(I_N(x,y) | j = \{0,1\})$$

- edge term

$$V(L(x,y), L(x',y')) = \eta(L(x,y), L(x',y')) \times \exp\left(-\frac{[I_N(x,y) - I_N(x',y')]}{2\sigma_L^2}\right)$$

with $\eta = [\![L(x,y) \neq L(x',y')]\!]$

Binarization results



Seed detection

- LoG filter $\mathrm{LoG}_{\mathrm{norm}}(x, y; \sigma) = \sigma^2 \, \mathrm{LoG}(x, y; \sigma)$

$$\mathrm{LoG}(x, y; \sigma) = \frac{\partial^2 G(x, y; \sigma)}{\partial x^2} + \frac{\partial^2 G(x, y; \sigma)}{\partial y^2}$$

- multiscale

$$R_N(x, y) = \underset{\sigma \in [\sigma_{\mathrm{min}}, \sigma_{\mathrm{MAX}}]}{\arg\max} \{\mathrm{LoG}_{\mathrm{norm}}(x, y; \sigma) * I_N(x, y)\}$$

where $\sigma_{\mathrm{MAX}} = \max\{\sigma_{\mathrm{min}}, \min\{\sigma_{\mathrm{max}}, 2 \times D_N(x, y)\}\}$.

D_N is a distance map

- seeds = local maxima, impose minimum size
- local-maximum clustering

Segmentation refinement

- Segment individual cells
- GraphCuts, α-expansion

$$V(L(x,y),L(x',y')) = \eta(L(x,y),L(x',y')) \times \exp(-|I_N(x,y) - I_N(x',y')|)$$

where

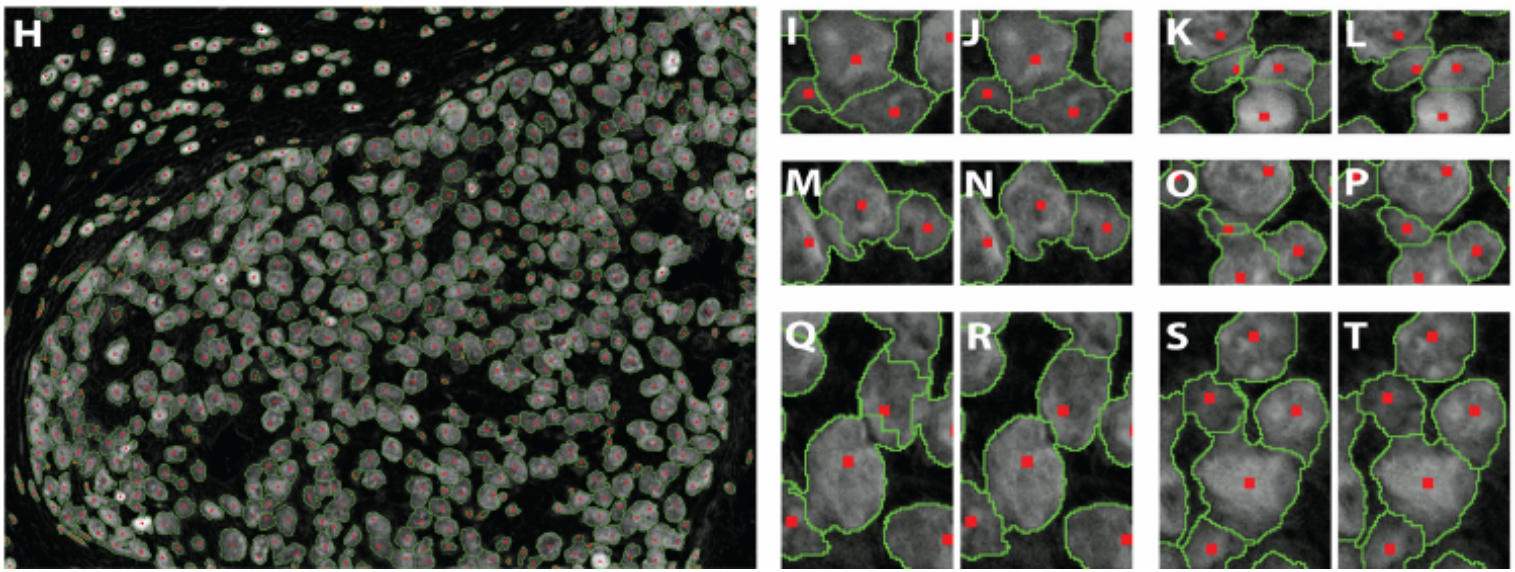
$$\eta(L(x,y),L(x',y')) = \begin{cases} \text{Const}, & \text{if } L(x,y) \neq L(x',y') \\ 0, & \text{if } L(x,y) = L(x',y'). \end{cases}$$

- Unary term - log likelihood for a Gaussian shape model $G(x, y; \mu_i, \Sigma_i)$

(x, y) pixels with LoG weights

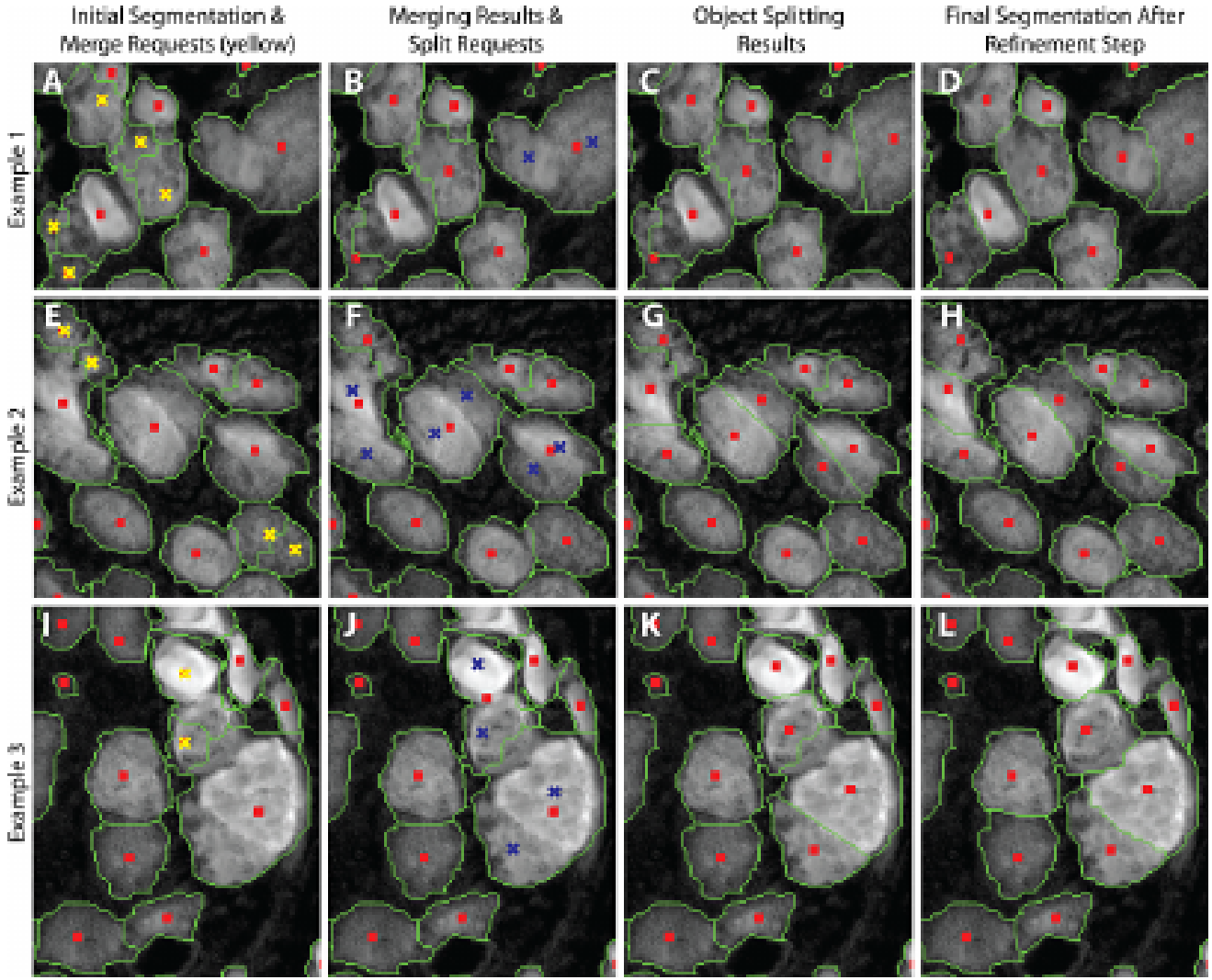
- to speed-up, group cells by graph colouring (e.g. 8 colors for 123 cells)
- iterate until convergence

Segmentation results

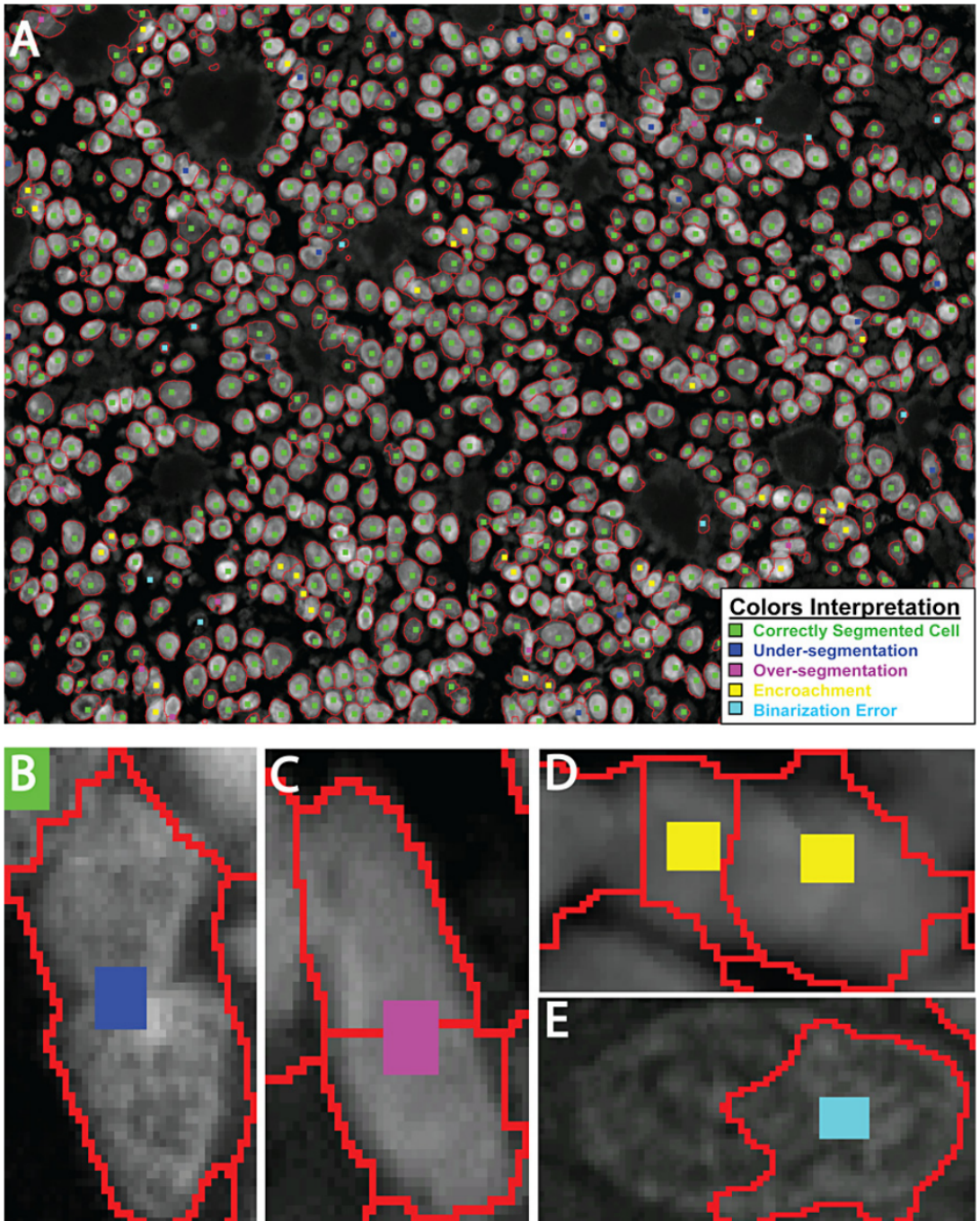


Computer-Assisted Editing

- merging, splitting, automatic refinement



Results


A
Colors Interpretation
Correctly Segmented Cell
Under-segmentation
Over-segmentation
Encroachment
Binarization Error
B
C
D
E

Results (2)