### **Proof Corrections**

### Joshua Vogelstein

May 22, 2009

Items are enumerated as in the faxed document.

### 1 Main article errors

- 1. Remove the word "the"
- 2. Replace"significant recent progress" with "significant progress recently"
- 3. Replace "Earlier this year" with "Last year"
- 4. Two comments on Equation (2)
  - Break this equation (into multiple lines) at the =
  - Replace  $\varepsilon_t$  with  $\varepsilon_{c,t}$
- 5. Replace "tth" with "t-th"
- 6. It seems as if in  $[Ca^{2+}]_b$ , the "b" is bold. It should not be.
- 7. Replace "referred to as" with "called"
- 8. Replace "i)" and "ii)" with "(i)" and "(ii)", respectively
- 9. Replace  $\frac{def}{=}$  with  $\stackrel{def}{=}$ , ie, the "=" should be in line with the rest of the equation, and the "def" should be just above it in a smaller font. This is a recurring problem.
- 10. Same as 9
- 11. Multiple comments on Equation (6)
  - Same as 9
  - Replace stuff after = with

$$\begin{cases} \mathcal{N}\big([\mathsf{C}\mathsf{a}^{2+}]_t; \widehat{\mu}(n_t), \sigma_c^2 \Delta\big)(p\Delta) & \text{if } n_t = 1\\ \mathcal{N}\big([\mathsf{C}\mathsf{a}^{2+}]_t; \widehat{\mu}(n_t), \sigma_c^2 \Delta\big)(1 - p\Delta) & \text{otherwise,} \end{cases}$$

- Try to fit within a single column, given the above substitution
- 12. Replace "Now the goal is to efficiently estimate  $P_{\theta}(\boldsymbol{H}_t|\boldsymbol{O}_{1:T}) = P_{\theta}(n_t, [\mathsf{Ca}^{2+}]_t \mid F_{1:T})$  for all t, the posterior distribution of the hidden signals, given all the observations." with "Now the goal is to efficiently estimate  $P_{\theta}(\boldsymbol{H}_t|\boldsymbol{O}_{1:T}) = P_{\theta}(n_t, [\mathsf{Ca}^{2+}]_t \mid F_{1:T})$ , the posterior distribution of the hidden signals, given all the observations, for all t."
- 13. Replace " $P_{\theta(H_t|O_{1:t})}$ " with " $P_{\theta}(H_t|O_{1:t})$ ", ie, only the  $\theta$  gets subscripted.

14. In Equation (9), after the final =, it should read:

$$P_{\theta}(F_t \mid [Ca^{2+}]_t^{(i)})P_{\theta}([Ca^{2+}]_t^{(i)} \mid [Ca^{2+}]_{t-1}^{(i)}, n_t^{(i)})P_{\theta}(n_t^{(i)})/Z,$$

The only acceptable places to put line breaks are between the ")"'s and "P"'s.

- 15. Replace " $\{n_t, [Ca^{2+}]_t\}$ " with " $n_t$  or  $[Ca^{2+}]_t$ "
- 16. Two remakrs about Equation (12)
  - ullet Replace  $\dfrac{{
    m argmax}}{oldsymbol{ heta}}$  with  ${
    m argmax}$

(note that argmax goes in line with the rest of the text, and  $\theta$  goes below it in a smaller font, similar to 9).

- Note that the  $\theta$  should be in bold.
- The "," should be after the final ")", not before
- 17. The " $\theta$ '" should be " $\theta$ '", ie, bold.
- 18. Replace "variance" with "noise term"
- 19. Remove "Main Result."
- 20. Remove sentence "Note that... of generality."
- 21. See 9
- 22. Repalce " $(q(\boldsymbol{H}_t) = P_{\boldsymbol{\theta}}(\boldsymbol{H}_t^{(i)}|\boldsymbol{H}_{t-1}^{(i)}, \boldsymbol{O}_t)$ )" with ",  $q(\boldsymbol{H}_t) = P_{\boldsymbol{\theta}}(\boldsymbol{H}_t^{(i)}|\boldsymbol{H}_{t-1}^{(i)}, \boldsymbol{O}_t)$ ,"
- 23. Replace " $(n_{1:T})$ " with ",  $n_{1:T}$ " and " $(\tau)$ " with ",  $\tau$ ,"
- 24. Remove "Saturated simulation."
- 25. Replace " $\xi=4\times 10^{-4}$  a.u." with " $\xi=4\times 10^{-4}~\mu$ A/photon, and replace  $\sigma_F=10^{-4}$  a.u." with " $\sigma_F=10^{-4}~\mu$ A"
- 26. Remove "In vitro bursts."
- 27. Replace "i)" with "(i)"
- 28. Remove "Real data saturation"
- 29. Replace and "ii)" with "(ii)"
- 30. Add the word "its" between "zero with" and "time constant"
- 31. Remove "Array of inferences."
- 32. Remove "Generalized linear model particle filter smoother."
- 33. Remove "In vitro data superresolution"
- 34. Replace "PFS both improves inference accuracy over the optimal linear method and provides" with "PFS both (i) improves inference accuracy over the optimal linear method and (ii) provides"
- 35. Replace " $\{\alpha, \beta, \sigma_F\}$ " with " $\{\alpha, \beta, \xi, \sigma_F\}$ "
- 36. Replace "i)" with "(i)" and "ii)" with "(ii)"

## 2 Appendix errors

- 1. Two things
  - See 9
  - Break at =
- 2. Break into two lines if possible
- 3. Try to into two lines
- 4. Replace " $\{[Ca^{2+}]_{t-1}\}^{(i)}$ " with " $[Ca^{2+}]_{t-1}^{(i)}$ "
- 5. Equation (34) should be rewritten as below. Note the location of the line break

$$g'(x) = \left(\frac{k_d(\beta - F_t)}{F_t - \beta - \alpha}\right)^{1/n} \frac{nk_d(\beta - F_t)}{F - \beta - \alpha}$$

$$\left(-\frac{k_d}{F-\beta-\alpha}-\frac{k_d(\beta-F_t)}{(F_t-\beta-\alpha)^2}\right).$$

- 6. Replace "are function of all the parameters:  $\alpha, \beta, \xi, \sigma_F, n$  and  $k_d$ " with "are function of  $\{\alpha, \beta, \xi, \sigma_F, n, k_d\}$ "
- 7. Line break after = sign
- 8. Two things
  - See 9
  - Replace cent sign with  $\mathbb{Z}$
- 9. Replace 'with  $\mathbb{Z}$
- 10. Remove "Laplace ... distribution."
- 11. Replace "The circles" with "The filled circles"
- 12. Line beginning with  $q_{\theta}^{S}$  should not be indented
- 13. (10) and (11) should not be links to references, they are sequences
- 14. Remove "Sampling strategies:" and capitalize "the"
- 15. (10) is a sequence, not a reference, no link
- 16. Remove "Mixture approximation:" and capitalize "appropriate"
- 17. "Computing..." should be a one level down in the heading hierarchy
- 18. This equation should not have a line break where the second line break is. I suggest:

$$\begin{split} P_{\pmb{\theta}}^{NL}(F_v \mid [\mathsf{Ca}^{2+}]_{v-1}) &= \sum_{n=0,1} a_{n,v-1} \\ & \int P_{\pmb{\theta}}^{NL}(F_v \mid [\mathsf{Ca}^{2+}]_v) P_{\pmb{\theta}}([\mathsf{Ca}^{2+}]_v \mid [\mathsf{Ca}^{2+}]_{v-1}, n_v = n) d[\mathsf{Ca}^{2+}]_v, \end{split}$$

or

$$P_{\theta}^{NL}(F_v \mid [\text{Ca}^{2+}]_{v-1}) = \sum_{n=0,1} a_{n,v-1} \int P_{\theta}^{NL}(F_v \mid [\text{Ca}^{2+}]_v)$$

$$P_{\theta}([\text{Ca}^{2+}]_v \mid [\text{Ca}^{2+}]_{v-1}, n_v = n) d[\text{Ca}^{2+}]_v,$$

- 19. " $a_{1, v-1}$ " should be " $a_{1,v-1}$ ", ie, there seems to be a space between the comma and the 'v', which should not be present. same is true for  $a_{0,v-1}$ . This problem repeats in several places
- 20. Indenting is totally inappropriate. Please use:

$$P_{\theta}([\mathsf{Ca}^{2+}]_v \mid [\mathsf{Ca}^{2+}]_{v-1}, n_v) = \\ \mathcal{N}([\mathsf{Ca}^{2+}]_v; [\mathsf{Ca}^{2+}]_{v-1} - \Delta/\tau([\mathsf{Ca}^{2+}]_{v-1} - [\mathsf{Ca}^{2+}]_b) + An_v, \sigma_c^2 \Delta),$$

21. Line break is again inappropriate. replace with

$$\begin{split} \int P_{\boldsymbol{\theta}}^{NL}(F_v \mid [\mathsf{Ca}^{2+}]_v) P_{\boldsymbol{\theta}}([\mathsf{Ca}^{2+}]_v \mid [\mathsf{Ca}^{2+}]_{v-1}, n_v &= n) d[\mathsf{Ca}^{2+}]_v \\ &= \int \mathcal{N}\big([\mathsf{Ca}^{2+}]_v; \widetilde{\mu}_v, \widetilde{\sigma}_v^2\big) \times \mathcal{N}([\mathsf{Ca}^{2+}]_v; [\mathsf{Ca}^{2+}]_{v-1} - \Delta/\tau([\mathsf{Ca}^{2+}]_{v-1} - [\mathsf{Ca}^{2+}]_b) + An_v, \sigma_c^2 \Delta). \end{split}$$

- 22. Replace  $\chi$  with  $C_v$
- 23. Replace  $\chi$  with  $C_v$
- 24. Line break should be:

$$\begin{split} P^{NL}_{\pmb{\theta}}(F_v \mid [\mathsf{Ca}^{2+}]_{v-1}) = \\ \sum_{n=0,1} a_{n,v-1} \mathcal{N}\left([\mathsf{Ca}^{2+}]_{v-1}; \widetilde{\mu}^S_v(n), (\widetilde{\sigma}^S_v)^2\right), \end{split}$$

25. Line break inappropriate. Replace with:

$$\begin{split} P_{\pmb{\theta}}^{NL}(F_v \mid [\mathsf{Ca}^{2+}]_{t-1}) = \\ \sum_{n=0}^{\infty} a_{n,t-1} \sum_{m=1}^{2^{v-t}} a_{mt} \mathcal{N}\left([\mathsf{Ca}^{2+}]_{t-1}; \widetilde{\mu}_{mt}^S(n), (\widetilde{\sigma}_t^S)^2\right), \end{split}$$

- 26. "Superresolution sampling spikes" should be one level down in hierarchy, ie, it should be indented
- 27. Replace  $n_t^{(i)}$  with  $n_t^{(i)}$ , ie, the (i) should be directly above t, not off to the side. this happens in 3 places on this line, and elsewhere
- 28. "Superresolution..." should be indented, just as 26
- 29. See 27
- 30. See 27 (twice on this line)
- 31. Line break is inappropriate, move it to after =
- 32. Same as 19
- 33. Same as 19
- 34. Two comments on this equation

in both instances (ie, argmax goes in line with the rest,  $\{b, k, \omega\}$  goes under in a smaller font

• (61) should be on the bottom line, not the middle one

35. Replace 
$$\tau$$
,  $A$ ,  $[Ca^{2+}]_b$ ,  $\sigma_c$  with

$$\underset{\tau,A,[\operatorname{Ca}^{2+}]_{b}\geq0}{\operatorname{argmax}}$$

- . Note a few differences
- (a) argmax is inline with rest of text, the other stuff is below
- (b)  $\sigma_c$  has been replaced with  $\leq$
- 36. Again, argmin should go inline, x > 0 should go underneath. equation should look like

$$\widehat{\boldsymbol{x}} = \operatorname*{argmin}_{\boldsymbol{x}>0} \frac{1}{2} \boldsymbol{x}' \boldsymbol{Q} \boldsymbol{x} + \boldsymbol{L}' \boldsymbol{x},$$

- 37. Remove ×
- 38. Same deal again with the argmin, equation should look like:

$$\widehat{\boldsymbol{x}} = \frac{1}{2} \underset{\boldsymbol{x}_p \geq 0, \forall p}{\operatorname{argmin}} \sum_{t=1}^{T} \sum_{i,j=1}^{N} J_{t,t-1}^{(i,j)} \left\| \boldsymbol{C}_t^{(i,j)} \boldsymbol{x} + d_t^{(i,j)} \right\|_2^2,$$

39. Again with the argmax, (69a) should look like

$$\widehat{\sigma_c}^2 = \operatorname*{argmax}_{\sigma_c^2} \sum_{t=1}^T \sum_{i,j=1}^N J_{t,t-1}^{(i,j)} \Bigg( -\frac{1}{2} \ln(2\pi \sigma_c^2 \Delta)$$

$$-\frac{1}{2} \frac{\left( [\mathsf{Ca}^{2+}]_t^{(i)} - \mu_{t,t-1}^{(i,j)} \right)^2}{\sigma_c^2 \Delta} \right)$$

40. Same with argmin, equation should look like

$$\{\widehat{\alpha}, \widehat{\beta}\} = \underset{\alpha, \beta \geq 0}{\operatorname{argmin}} \sum_{t=1}^{T} \sum_{i=1}^{N} \frac{(F_t - \alpha S([\operatorname{Ca}^{2+}]_t) - \beta)^2}{\xi S([\operatorname{Ca}^{2+}]_t) + \sigma_F}$$

$$+\ln\left(\xi S([\operatorname{Ca}^{2+}]_t)+\sigma_F\right),$$

41. Another problem with argmin, equation should look like

$$\{\widehat{\xi}, \widehat{\sigma_F}\} = \underset{\xi, \sigma_F \ge 0}{\operatorname{argmin}} (r_t - \xi S([\operatorname{Ca}^{2+}]_t) - \sigma_F)^2,$$

# 3 response to inquiries

- 1. ok.
- 2. ok.
- 3. ok.
- 4. See [Yuste and Konnerth, 2006]
- 5. See [Tay et al., 2007]
- 6. See [Yasuda et al., 2004]
- 7. See [Borst and Abarbanel, 2007]
- 8. See [Sasaki et al., 2008]
- 9. See [Smith et al., 2001]
- 10. See [Dempster et al., 1977]
- 11. See [Samejima et al., 2004]
- 12. This is correct. NIPS is a conference proceedings.
- 13. Please replace with [Huys and Paninski, 2009]
- 14. Maybe also look for Transactions of the ASME, as in [Kalman, 1960]
- 15. Please replace with [Huys and Paninski, 2009]
- 16. Journal title is "Network: Computation in Neural Systems", as suggested by [Paninski et al., 2004]
- 17. See [Vogelstein et al., 2009]
- 18. See [Pillow et al., 2008]
- 19. See [Shumway and Stoffer, 2006]
- 20. Replace "To sample conditioned on the next observation" with "To sample  $\{n_t, [Ca^{2+}]_t\}$  conditioned on the next observation"

REFERENCES REFERENCES

### References

[Borst and Abarbanel, 2007] Borst, A. and Abarbanel, H. D. I. (2007). Relating a calcium indicator signal to the unperturbed calcium concentration time-course. *Theor Biol Med Model*, 4(1):7.

- [Dempster et al., 1977] Dempster, A., Laird, N., Rubin, D., et al. (1977). Maximum likelihood from incomplete data via the EM algorithm. *Journal of the Royal Statistical Society. Series B (Methodological)*, 39(1):1–38.
- [Huys and Paninski, 2009] Huys, Q. and Paninski, L. (2009). Smoothing of, and Parameter Estimation from, Noisy Biophysical Recordings. *PLoS Comput Biol*, 5(5):e1000379.
- [Kalman, 1960] Kalman, R. (1960). A new approach to linear filtering and prediction problems. *Transactions of the ASME Journal of Basic Engineering*, 82(1):35–45.
- [Paninski et al., 2004] Paninski, L., Pillow, J. W., and Simoncelli, E. P. (2004). Maximum likelihood estimation of a stochastic integrate-and-fire neural encoding model. *Neural Computation*, 16(12):2533–2561.
- [Pillow et al., 2008] Pillow, J., Shlens, J., Paninski, L., Sher, A., Litke, A., Chichilnisky, E., and Simoncelli, E. (2008). Spatiotemporal correlations and visual signaling in a complete neuronal population. *Nature*, 454(7207):995–9.
- [Samejima et al., 2004] Samejima, K., Doya, K., Ueda, Y., and Kimura, M. (2004). Estimating internal variables and parameters of a learning agent by a particle filter. *Advances in Neural Information Processing Systems*, 16.
- [Sasaki et al., 2008] Sasaki, T., Takahashi, N., Matsuki, N., and Ikegaya, Y. (2008). Fast and accurate detection of action potentials from somatic calcium fluctuations. *Journal of Neurophysiology*, 100(3):1668.
- [Shumway and Stoffer, 2006] Shumway, R. and Stoffer, D. (2006). *Time Series Analysis and Its Applications*. Springer, New York, NY, 2nd edition.
- [Smith et al., 2001] Smith, A., Doucet, A., de Freitas, N., and Gordon, N. (2001). *Sequential Monte Carlo Methods in Practice*. Springer, New York.
- [Tay et al., 2007] Tay, L. H., Griesbeck, O., and Yue, D. T. (2007). Live-Cell Transforms between Ca<sup>2+</sup> Transients and FRET Responses for a Troponin-C-Based Ca<sup>2+</sup> Sensor. *Biophys J*, 93(11):4031–4040.
- [Vogelstein et al., 2009] Vogelstein, J., Packer, A., Yuste, R., and Paninski, L. (2009). Towards inferring neural circuits from population calcium imaging. *Frontiers in Systems Neuroscience. Conference Abstract: Computational and systems neuroscience*.
- [Yasuda et al., 2004] Yasuda, R., Nimchinsky, E. A., Scheuss, V., Pologruto, T. A., Oertner, T. G., Sabatini, B. L., and Svoboda, K. (2004). Imaging calcium concentration dynamics in small neuronal compartments. *Sci STKE*, 2004(219):pl5.
- [Yuste and Konnerth, 2006] Yuste, R. and Konnerth, A. (2006). *Imaging in Neuroscience and Development, A Laboratory Manual*.