Appendix A: Semi-infinite Solution for Diffuse Speckle Contrast Resulted from Scatterer's Brownian Motion

Speckle contrast for monitoring flow variations can be calculated by [1]

$$K_s(\boldsymbol{r}) = \frac{\sigma_s}{\langle I \rangle} \qquad \text{(A.1)}$$

where the spatial (or temporal) standard deviation, σ_s, and mean intensity, $\langle I \rangle$, are from a chosen camera pixel region at detection position $\boldsymbol{r}$. The speckle contrast can be related to the normalized electric field temporal autocorrelation function, $g_1(\boldsymbol{r}, \tau)$ by [2]

$$K_s^2(\boldsymbol{r}) = \frac{2\beta}{T}\int_0^T \left(1 - \frac{\tau}{T}\right) g_1^2(\boldsymbol{r}, \tau) d\tau \qquad \text{(A.2)}$$

with exposure time T, correlation delay time τ, and β relating detector and speckle sizes.

The correlation diffusion equation (CDE), as presented in diffuse correlation spectroscopy (DCS) theory, acts to both model the transport of the unnormalized electric field temporal autocorrelation function, G_1, through biological tissues and enable the introduction of system and sample parameters. The analytic solution in the case of semi-infinite geometry with continuous-wave light source is [3]

$$G_1(\boldsymbol{r}, \tau) = \frac{vS_0}{4\pi D}\left(\frac{e^{-r_1 M}}{r_1} - \frac{e^{-r_2 M}}{r_2}\right) \qquad \text{(A.3)}$$

where $M^2 = 3\mu_a\mu_s' + {\mu_s'}^2 k_0^2 \alpha \Delta r^2(\tau)$ with $\Delta r^2(\tau) = 6D_B\tau$ for particle Brownian motion, τ is correlation decay time, $r_1 = \sqrt{\rho^2 + (z - z_0)^2}$, $r_2 = \sqrt{\rho^2 + (z + z_0 + 2z_b)^2}$, $z_0 = 1/\mu_s{'}$, $z_b = 2(1 + R_{eff})/3\mu_s'(1 - R_{eff})$, $R_{eff} = -1.440n^{-2} + 0.710n^{-1} + 0.0636n + 0.668$ accounts for the refractive index mismatch between air and the medium, $n \approx 1.33$ for both the phantoms and tissues, $\rho = |\boldsymbol{r} - \boldsymbol{r}_s|$ is the source-detector (S-D) separation with source position $\boldsymbol{r}_s$ on the sample surface, k_0 is the wavenumber, $D = \frac{v}{3(\mu_a + \mu_s')} \approx \frac{v}{3\mu_s'}$, S_0 is the source term, v is the velocity of light in the medium, and μ_a and μ_s' are the respective absorption and reduced scattering coefficients of the medium. The αD_B term is collectively referred to as the blood flow index, BFI, and involves the effective diffusion coefficient of moving scatterers, D_B, and α which accounts for the ratio of dynamic to static scatterers. Normalizing to $G_1(\boldsymbol{r}, \tau = 0)$, we obtain

$$g_1(\boldsymbol{r}, \tau) = C[r_2 e^{-r_1 M} - r_1 e^{-r_2 M}] \qquad \text{(A.4)}$$

where $C = \left(r_2 e^{-r_1\sqrt{3\mu_a\mu_s'}} - r_1 e^{-r_2\sqrt{3\mu_a\mu_s'}}\right)^{-1}$. Inserting (A.4) into (A.2),

$$K_s^2(\boldsymbol{r}) = \frac{2\beta C^2}{T}\Big[\int_0^T \left(r_1^2 e^{-2r_2 M} - 2r_1 r_2 e^{-(r_1 + r_2)M} + r_2^2 e^{-2r_1 M}\right) d\tau$$
$$- \frac{1}{T}\int_0^T \tau\left(r_1^2 e^{-2r_2 M} - 2r_1 r_2 e^{-(r_1 + r_2)M} + r_2^2 e^{-2r_1 M}\right) d\tau\Big] \qquad \text{(A.5)}$$

which after rewriting τ in terms of M as

$$\tau = \frac{M^2 - 3\mu_a\mu_s'}{6{\mu_s'}^2 k_0^2 \alpha D_B} \qquad \text{(A.6)}$$

and

$$d\tau = \frac{M}{3{\mu_s'}^2 k_0^2 \alpha D_B} d\text{M} \qquad \text{(A.7)}$$

we can consider the integrals of the following two general forms with their corresponding solutions

$$A = \frac{1}{3{\mu_s'}^2 k_0^2 \alpha D_B}\sum_{i=1}^3 x_i \int_a^b M e^{y_i M} dM = \frac{1}{3{\mu_s'}^2 k_0^2 \alpha D_B}\sum_{i=1}^3 \left(\frac{x_i}{y_i^2}\right)[(y_i b - 1)e^{y_i b} - (y_i a - 1)e^{y_i a}] \quad \text{(A.8)}$$

and

$$B = \frac{1}{18{\mu_s'}^4 k_0^4 (\alpha D_B)^2}\sum_{i=1}^3 x_i \int_a^b (M^2 - 3\mu_a\mu_s') M e^{y_i M} dM$$

$$= \frac{1}{18{\mu_s'}^4 k_0^4 (\alpha D_B)^2} \sum_{i=1}^{3} \left(\frac{x_i}{y_i^4}\right) [({y_i}^3 b^3 - 3{y_i}^2 b^2 - {y_i}^3 b a^2 + 6 y_i b + {y_i}^2 a^2 - 6) e^{y_i b} + 2({y_i}^2 a^2 - 3 y_i a + 3) e^{y_i a}] \quad \text{(A.9)}$$

with $x_i = \begin{cases} r_1^2 & i = 1 \\ -2r_1 r_2 & i = 2 \\ r_2^2 & i = 3 \end{cases}$, $y_i = \begin{cases} -2r_2 & i = 1 \\ -(r_1 + r_2) & i = 2 \\ -2r_1 & i = 3 \end{cases}$, $a = \sqrt{3\mu_a \mu_s'}$ and $b = \sqrt{6{\mu_s'}^2 k_0^2 \alpha D_B T + 3\mu_a \mu_s'}$. The final solution is then

$$K_s^2(\boldsymbol{r}) = \frac{2\beta C^2}{T}\left[A - \frac{1}{T}B\right] \quad . \quad \text{(A.10)}$$

The theoretical diffuse speckle contrast can be seen to be a function of several parameters, explicitly $K_s^2(\boldsymbol{r}) = f(\alpha D_B, T, \mu_a, \mu_s', \lambda, \beta, k_0, \boldsymbol{r})$. We assume that all parameters remain constant throughout the camera integration time. All parameters are known, measurable, or estimated from literature except for αD_B (i.e., the blood flow index, BFI). We proceed to determine the BFI in the following fashion. The experimentally measured diffuse speckle contrast is calculated from CCD camera measurements by (A.1) with noise corrections, which we term K_{se}^2 for illustrative purposes. The theoretical diffuse speckle contrast is calculated by (A.10), similarly termed K_{st}^2. As BFI is unknown, we finally minimize the squared difference between the two speckle contrasts, $\min_{\alpha D_B}(K_{se}^2 - K_{st}^2)^2$, with respect to BFI.

References

[1] A. F. Fercher and J. D. Briers, "Flow Visualization by Means of Single-Exposure Speckle Photography," *Optics Communications,* vol. 37, no. 5, pp. 326-330, 1981.

[2] R. Bandyopadhyay, A. S. Gittings, S. S. Suh, P. K. Dixon, and D. J. Durian, "Speckle-visibility spectroscopy: A tool to study time-varying dynamics," *Review of Scientific Instruments,* vol. 76, no. 9, Sep 2005.

[3] C. Zhou, "In-vivo optical imaging and spectroscopy of cerebral hemodynamics," Ph.D. thesis, University of Pennsylvania, Dissertation, 2007.