

Firing-rate response of a neuron receiving excitatory and inhibitory synaptic shot noise

Supplementary material

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I. THRESHOLD INTEGRATION FOR SHOT-NOISE PROCESSES WITH A BOUNDARY

Rate-based quantities for additive, exponentially distributed shot-noise processes can be derived using Laplace transforms. However, voltage-dependent quantities like the probability density are less conveniently derived. Furthermore, detailed models of neuronal integration which include reversal potentials or non-linear spike mechanisms are not amenable to a Laplace transform approach, even for rate-based quantities. The Threshold Integration method recently developed for non-linear neurons receiving Gaussian white noise [1, 2] provides a simple numerical scheme for integrating threshold-reset systems and can be readily adapted to the case of shot noise. The steady state for additive noise treated in this paper will be used as an example. The continuity and synaptic flux equations are

$$\partial_v J = -\partial_t P + r(t) (\delta(v - v_{re}) - \delta(v - v_{th})) \quad (1)$$

$$\partial_v J_e = -J_e/a_e + R_e P - r(t)\delta(v - v_{th}) \quad (2)$$

$$\partial_v J_i = -J_i/a_i + R_i P + J_i(v_{lb})\delta(v - v_{lb}) \quad (3)$$

where $P = \tau(J_e + J_i - J)/v$. The last term in the flux equation for J_i restricts the voltage to be between a lower bound v_{lb} and threshold v_{th} for numerical convenience (if v_{lb} is set sufficiently low it has a negligible effect on the results). In the steady state the system of equations (1,2,3) reduces to three coupled first-order differential equations with two inhomogeneous terms: one proportional to r_0 and another to $J_{i0}(v_{lb})$ both of which are *a priori* unknown. Resolving the solution into two components proportional to these terms $J_0 = r_0 f_0 + |J_{i0}(v_{lb})|g_0$ and similarly for J_{e0} , J_{i0} yields two equation sets. For cases where $v_{re} > 0$ the first set

$$\partial_v f_0 = \delta(v - v_{re})$$

$$\partial_v f_{e0} = -f_{e0}/a_e + \tau R_{e0}(f_{e0} + f_{i0} - f_0)/v$$

$$\partial_v f_{i0} = -f_{i0}/a_i + \tau R_{i0}(f_{e0} + f_{i0} - f_0)/v$$

is integrated backwards from $v_{th} \rightarrow 0_+$ with initial conditions $f_0(v_{th}) = f_{e0}(v_{th}) = 1$ and $f_{i0} = 0$. The second set

$$\partial_v g_0 = 0$$

$$\partial_v g_{e0} = -g_{e0}/a_e + \tau R_{e0}(g_{e0} + g_{i0} - g_0)/v$$

$$\partial_v g_{i0} = -g_{i0}/a_i + \tau R_{i0}(g_{e0} + g_{i0} - g_0)/v$$

is integrated forwards from $v_{lb} \rightarrow 0_-$ with initial conditions $g_0(v_{lb}) = g_{e0}(v_{lb}) = 0$ and $g_{i0} = -1$. The functions are matched on either side of $v = 0$ by enforcing $J_{e0}(0_-) = J_{e0}(0_+)$

$$|J_{i0}(v_{lb})|g_{e0}(0_-) = r_0 f_{e0}(0_+) \quad (4)$$

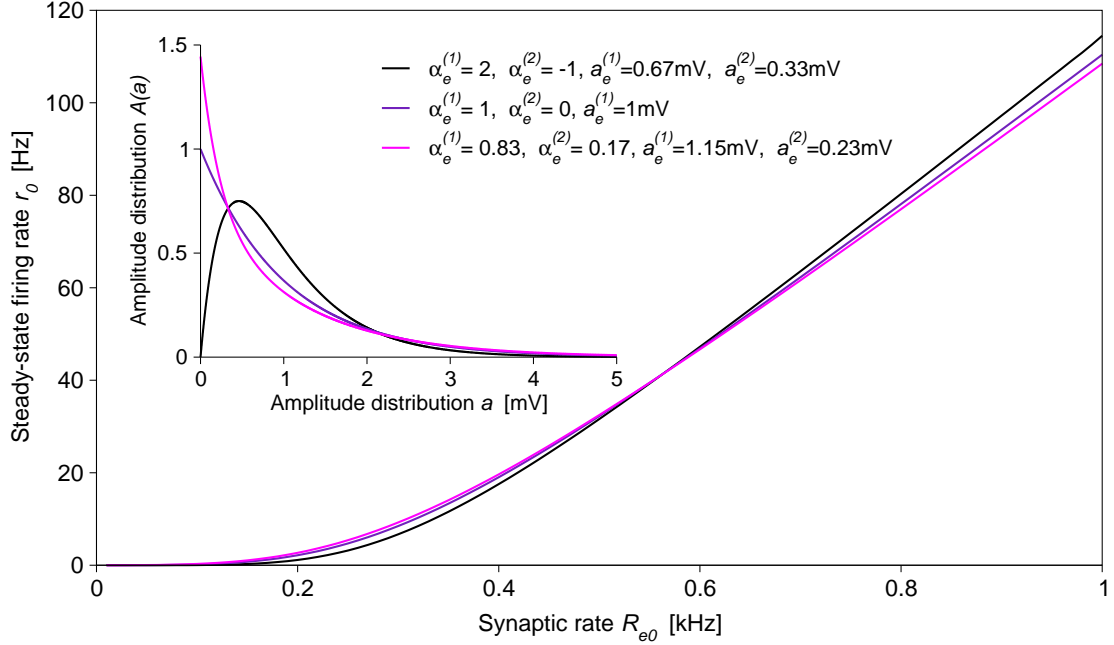


Figure 1: Generalized amplitude distributions: steady-state firing rate as a function of the synaptic rate. The inset shows the three example distributions (one is a single exponential $\alpha_e^{(2)}=0$ for comparison). For each distribution the parameters (marked on the figure) have been chosen so that the average synaptic amplitude is 1mV, leading (in this case) to similar steady-state firing-rate profiles despite the different underlying amplitude distributions. Other parameters were $\tau=20\text{ms}$, $v_{re}=5\text{mV}$ and $v_{th}=10\text{mV}$.

which is rearranged to yield $|J_{i0}(v_{lb})|/r_0 = f_{e0}(0_+)/g_{e0}(0_-)$. Normalization of the probability density $P_0 = \tau(J_{e0} + J_{i0} - J_0)/v$ is then used to extract r_0

$$\frac{1}{\tau r_0} = \int_{v_{lb}}^{v_{th}} \frac{dv}{v} \left((f_{e0} + f_{i0} - f_0) + \frac{|J_{i0}(v_{lb})|}{r_0} (g_{e0} + g_{i0} - g_0) \right) \quad (5)$$

and consequently $J_{i0}(v_{lb})$ to give the steady-state probability density and fluxes. It is straightforward to generalize the above for cases where $v_{re} < 0$.

II. GENERALIZED AMPLITUDE DISTRIBUTIONS

The framework developed for shot-noise processes with a single exponential amplitude distribution generalizes readily to distributions that can be written as sums of exponentials

$$A(a) = \sum_m \alpha^{(m)} \exp(-a/a^{(m)})/a^{(m)} \quad (6)$$

for $A_e(a)$ or $A_i(a)$. The prefactors $\alpha^{(m)}$ may be positive or negative as long as the distribution is always positive and the normalization is chosen so that $\sum_m \alpha^{(m)} = 1$. A full description of the analytical solution for the generalized case, which can be obtained straightforwardly using the Laplace-transform approach, is beyond the scope of this Letter. However, we provide (using the numerical Threshold Integration method) an example

case: the two-component excitatory process. The equations to be solved are

$$\partial_v J_0 = (r_0^{(1)} + r_0^{(2)}) (\delta(v - v_{re}) - \delta(v - v_{th})) \quad (7)$$

$$\partial_v J_{e0}^{(1)} + J_{e0}^{(1)}/a_e^{(1)} = R_{e0}^{(1)} P_0 - r_0^{(1)} \delta(v - v_{th}) \quad (8)$$

$$\partial_v J_{e0}^{(2)} + J_{e0}^{(2)}/a_e^{(2)} = R_{e0}^{(2)} P_0 - r_0^{(2)} \delta(v - v_{th}) \quad (9)$$

$$J_0 = J_{e0}^{(1)} + J_{e0}^{(2)} - vP_0/\tau \quad (10)$$

where $R_{e0}^{(1,2)} = \alpha_e^{(1,2)} R_{e0}$ where R_{e0} is the total excitatory synaptic rate and $r_0^{(1)}$ and $r_0^{(2)}$ are the contributions of each component to the total steady-state rate $r_0 = r_0^{(1)} + r_0^{(2)}$. Note that the signs of $r_0^{(1,2)}$ depend on those of $\alpha_e^{(1,2)}$. The solutions of equations (7-10) are linear in each component's contribution to the firing rate and so must be of the form $J_0(r_0^{(1)}, r_0^{(2)}) = r_0^{(1)} J_0(1, 0) + r_0^{(2)} J_0(0, 1)$ and similarly for $J_{e0}^{(1)}$, $J_{e0}^{(2)}$ and P_0 . The solutions for the case (1, 0) are found using the Threshold Integration method, integrating from v_{th} backwards to 0, and similarly for the case (0, 1). The unknown rate components can then be found from the normalization and zero-flux requirement at the origin $J_e^{(1)}|_{v=0} = 0$ (or equivalently $J_e^{(2)}|_{v=0} = 0$ via Eq. 7)

$$1 = r_0^{(1)} \int_0^{v_{th}} P_0(1, 0) dv + r_0^{(2)} \int_0^{v_{th}} P_0(0, 1) dv \quad (11)$$

$$0 = r_0^{(1)} J_e^{(1)}(1, 0)|_{v=0} + r_0^{(2)} J_e^{(1)}(0, 1)|_{v=0} = 0 \quad (12)$$

where it is assumed that a case $v_{re} > 0$ is being considered. Example solutions for the steady-state rate for two-component distributions are shown in figure 1.

III. SPIKE-TRAIN SPECTRUM FOR A NEURON DRIVEN BY SYNAPTIC SHOT NOISE

The first-passage-time density for two-sided additive shot noise has recently been derived in the mathematics literature [3]. The closely related spike-train spectrum (STS) will now be derived here using the framework developed for the firing-rate response. The STS is the Fourier transform of the autocorrelation $C(T)$ of the spike train $S(t) = \sum_k \delta(t - t_k)$ where $\{t_k\}$ are the spike times of the neuron:

$$C(T) = \langle S(t)S(t+T) \rangle = r_0 (\delta(T) + \varrho(T)) \quad (13)$$

and where $\varrho(t)$ is the spike rate at time t given a spike at $t=0$. Its Fourier transform is therefore $\hat{C}(\omega) = r_0 (1 + 2\Re\hat{\varrho}(\omega))$. The continuity equation for this case is

$$\frac{\partial P}{\partial t} + \frac{\partial J}{\partial v} = \varrho(t) (\delta(v - v_{re}) - \delta(v - v_{th})) + \delta(t)\delta(v - v_{re}) \quad (14)$$

and the excitatory flux equation is $\partial_v J_e + J_e/a_e = R_e P - \varrho(t)\delta(v - v_{th})$. The inhibitory flux equation and total flux $J = J_e + J_i - vP/\tau$ are unchanged from those given in the paper. Fourier transforms in time and a bilateral Laplace transforms in voltage $\tilde{\phi}(s, \omega) = \int_{-\infty}^{\infty} dt e^{-i\omega t} \int_{-\infty}^{\infty} dv e^{sv} \phi(v, t)$ are performed on these equations and substitution for the transformed fluxes yields an equation for the transformed density \tilde{P}

$$\frac{d\tilde{P}}{ds} = \left(\frac{a_e \tau R_{e0}}{1 - a_e s} + \frac{a_i \tau R_{i0}}{1 - a_i s} - \frac{i\omega \tau}{s} \right) \tilde{P} + \frac{e^{sv_{re}} \tau}{s} - \frac{\tau \hat{\varrho}}{s} \left(\frac{e^{sv_{th}}}{1 - a_e s} - e^{sv_{re}} \right). \quad (15)$$

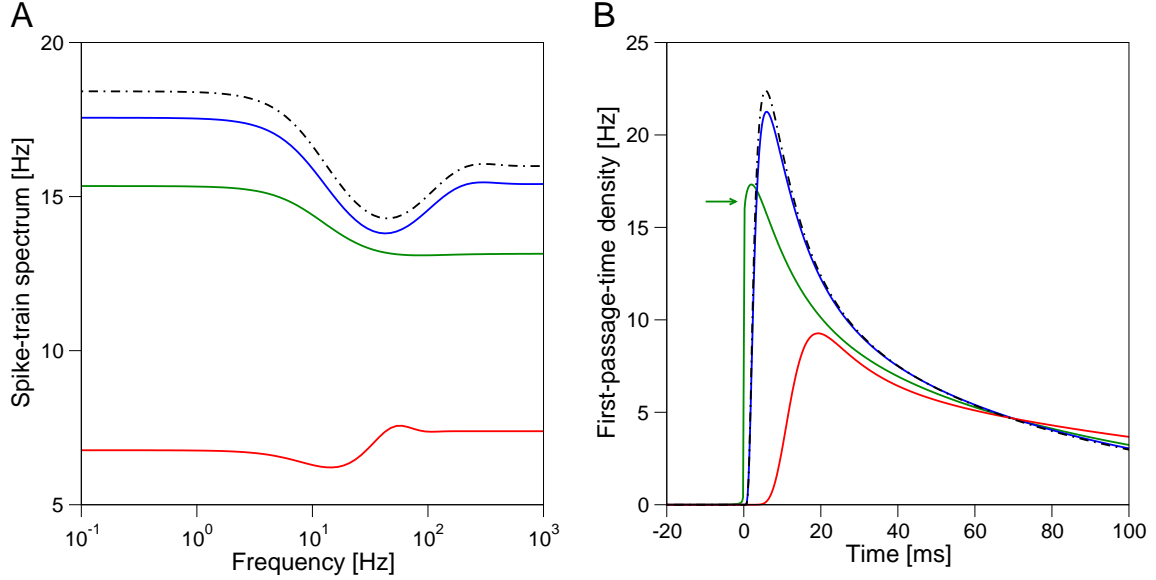


Figure 2: (A) Spike-train spectrum and (B) first-passage-time density [3] for a neuron receiving synaptic shot noise. The color scheme is the same as that used in the paper with the diffusion approximation in black.

From the initial conditions $\tilde{P}(s=0, \omega) = \pi\delta(\omega) + 1/i\omega$ and hence $\tilde{P}(s, \omega) - 1/i\omega \rightarrow 0$ in the limit $s \rightarrow 0$ (for non zero frequency). With this in mind, equation (15) is solved for $\tilde{P}(s, \omega) - 1/i\omega$ and integrated from 0 to $1/a_e$ so that terms featuring \tilde{P} vanish. After some rearranging, the Fourier transform of the spike-triggered rate can be written

$$\hat{\varrho}(\omega) = \frac{\int_0^{1/a_e} ds s^{i\omega\tau} \frac{d}{ds} \left[\frac{1}{Z_0(s)} e^{sv_{re}} \right]}{\int_0^{1/a_e} ds s^{i\omega\tau} \frac{d}{ds} \left[\frac{1}{Z_0(s)} \left(\frac{e^{sv_{th}}}{1-a_es} - e^{sv_{re}} \right) \right]} \quad (16)$$

for $\omega \neq 0$ where additionally $\hat{\varrho}(\omega=0) = r_0\pi\delta(\omega)$. It should be noted that this compact form involves a final partial-integration step for the integral in the denominator that is valid only for the biophysically interesting case where $R_{e0}\tau > 1$. The spike-train spectra for cases i, ii and iii treated in the paper are plotted in figure 2A. The result (16) is closely related to the Fourier transform of the first-passage-time density $f(t)$ [3] via $\hat{f} = \hat{\varrho}/(1+\hat{\varrho})$. The numerical inverse-transforms for the first-passage-time density are plotted in figure 2B. It is worth drawing attention to the initial value of the first-passage-time density (at $t=0$) for shot-noise synaptic drive. This can be obtained directly by considering the fraction of initial excitatory jumps across threshold from reset, so that $f(0) = R_{e0}e^{-(v_{th}-v_{re})/a_e}$ (see arrow in 2B for case i which has large excitatory amplitudes). This finite value is distinct from the diffusion-approximation prediction for which $f(0)=0$.

IV. NUMERICAL EVALUATION OF SHOT-NOISE INTEGRALS AT HIGH FREQUENCY

Many shot-noise quantities consist of the ratio of two integrals I_f/I_g of form

$$I_f = \int_0^{1/a_e} ds s^{i\omega\tau} (1-a_es)^{R_{e0}\tau} (1-a_is)^{R_{i0}\tau} f(s). \quad (17)$$

The presynaptic rate $R_{e0}\tau$ can be of-the-order-of 10^2 or higher for biophysically reasonable parameter ranges, concentrating the mass of the integrand near $s = 0$. However, when $w\tau \gg 1$ the integrand becomes increasingly oscillatory as $s \rightarrow 0$. Together, these features make integrals of the form (17) rather awkward to evaluate numerically at high frequencies. One method is to identify the saddle point of the first three terms in the integrand (common to both I_f and I_g), rotate the integration variable in the complex plane so that the numerical integration passes through this saddle point and include a divisive factor in the numerator and denominator integrals evaluated at the saddle point. To this end, the substitution $s = \exp(-x)/a_e$ is made

$$I_f = \frac{1}{a_e^{1+i\omega\tau}} \int_0^\infty dx e^{-x(1+i\omega\tau)} (1 - e^{-x})^{R_{e0}\tau} (1 - ae^{-x})^{R_{i0}\tau} f(e^{-x}/a_e) \quad (18)$$

where $a = a_i/a_e$. The saddle point is found by extremizing $\Psi(x)$ where

$$\Psi(x) = x(1 + i\omega\tau) - R_{e0}\tau \log(1 - e^{-x}) - R_{i0}\tau \log(1 - ae^{-x}). \quad (19)$$

which leads to a quadratic equation for e^x . The root $x = z^* = |z|^* e^{i\theta^*}$ which has a negative imaginary part is chosen. It is convenient to introduce the rotation $\phi^* = e^{i\theta^*}$ and continue the integral into the complex plane $x \rightarrow r\phi^*$ so that the ratio of integrals becomes

$$\frac{I_f}{I_g} = \frac{\int_0^\infty dr e^{-\Delta\Psi(r)} f(e^{-r\phi^*}/a_e)}{\int_0^\infty dr e^{-\Delta\Psi(r)} g(e^{-r\phi^*}/a_e)} \quad (20)$$

where $\Delta\Psi(r) = \Psi(r\phi^*) - \Psi(z^*)$. Integrals of the form $\int_0^\infty dr e^{-\Delta\Psi(r)} f(e^{-r\phi^*}/a_e)$ can be comfortably evaluated numerically up to frequencies of at least 10^6 Hz.

V. DIFFUSION APPROXIMATION SOLVED USING LAPLACE TRANSFORMS

The firing-rate response to modulated current [4] and variance [4, 5], as well as the spike-train spectrum [6] have been derived previously for the diffusion approximation in terms of hypergeometric functions. To provide convenient integral representations of these results the method of bilateral Laplace transforms is also applied to the diffusion approximation. For this case the voltage dynamics and flux equations are

$$\tau \frac{dv}{dt} = \mu - v + \sigma \sqrt{2\tau} \xi(t) \quad \text{and} \quad \tau J = (\mu - v)P - \sigma^2 \frac{dP}{dv} \quad (21)$$

with the continuity equation $\partial_t P + \partial_v J = r(t) (\delta(v - v_{re}) - \delta(v - v_{th}))$ identical to the shot-noise case. In the steady state a bilateral Laplace transform of the flux and continuity equations yields the following for the transformed density \tilde{P}_0

$$\frac{d\tilde{P}_0}{ds} = (\mu_0 + s\sigma_0^2) \tilde{P}_0 - \frac{\tau r_0}{s} (e^{sv_{th}} - e^{sv_{re}}). \quad (22)$$

This can be solved for \tilde{P}_0 and integrated between from $s \rightarrow \infty$ to yield

$$\tilde{P}_0 = \tau r_0 e^{\mu_0 s + \sigma_0^2 s^2 / 2} \int_s^\infty \frac{dx}{x} e^{-\mu_0 x - \sigma_0^2 x^2 / 2} (e^{xv_{th}} - e^{xv_{re}}) \quad (23)$$

which for $s=0$ gives the steady state rate as

$$\frac{1}{r_0\tau} = \int_0^\infty \frac{dy}{y} e^{-y^2/2} (e^{yy_{th}} - e^{yy_{re}}) \quad (24)$$

where $y_{th} = (v_{th} - \mu_0)/\sigma_0$ and analogously for y_{re} in agreement with reference [4]. The spike-train spectrum and Fourier-transform of the first-passage-time density can be derived using exactly the same method used for shot noise (see above). Defining an integral

$$A_{th} = \int_0^\infty dy y^{i\omega\tau} \frac{d}{dy} (e^{-y^2/2} e^{yy_{th}}) \quad (25)$$

and similarly for the reset v_{re} the Fourier transforms of the spike-triggered rate $\hat{\rho}$ (required for the spike-train spectrum defined in Eq. 13) and the first-passage-time density can be expressed simply as

$$\hat{\rho} = A_{re}/(A_{th} - A_{re}) \quad \text{and} \quad \hat{f} = A_{re}/A_{th} \quad (26)$$

which are integral representations of the results derived previously in terms of Cylinder functions [6].

Firing-rate response for the diffusion approximation. The firing-rate response to modulated current $\mu = \mu_0 + \mu_1 e^{i\omega\tau}$ or variance $\sigma^2 = \sigma_0^2 + \sigma_1^2 e^{i\omega\tau}$ can also be derived straightforwardly using Laplace transforms. The modulated flux is either

$$\tau J_1 = P_1(\mu_0 - v) - \sigma_0^2 \frac{dP_1}{dv} + P_0\mu_1 \quad \text{or} \quad \tau J_1 = P_1(\mu_0 - v) - \sigma_0^2 \frac{dP_1}{dv} - \sigma_1^2 \frac{dP_0}{dv} \quad (27)$$

for these two cases, respectively. Laplace transforming either of these equations and combining it with the transformed modulated continuity equation, and solving in the same way as for the shot-noise case allows the modulations to be expressed in terms of ratios of integrals of the form

$$B_m = \int_0^\infty \frac{dy}{y} y^{m+i\omega\tau} e^{-y^2/2} (e^{yy_{th}} - e^{yy_{re}}) \quad (28)$$

so that the rate response for current r_μ and variance can be written r_{σ^2}

$$r_\mu = \frac{r_0}{1 + i\omega\tau} \frac{\mu_1}{\sigma_0} \frac{B_1}{B_0} \quad \text{and} \quad r_{\sigma^2} = \frac{r_0}{2 + i\omega\tau} \frac{\sigma_1^2}{\sigma_0^2} \frac{B_2}{B_0} \quad (29)$$

which are integral representations of results derived previously in terms of hypergeometric functions [4, 5], though see the equation set A.19 of reference [4] for related integral representations. To compare with the shot-noise case the modulation of a presynaptic excitatory or inhibitory rate $R_{\kappa 1}$ (with $\kappa = e, i$) is given by $r_\kappa = r_\mu + r_{\sigma^2}$ with $\mu_1 = R_{\kappa 1} \tau a_\kappa$ and $\sigma_1^2 = R_{\kappa 1} \tau a_\kappa^2$.

Numerical evaluation of diffusion integrals at high frequencies. For diffusion-approximation quantities, ratios of integrals I_f/I_g of form

$$I_f = \int_0^\infty dy y^{i\omega\tau} e^{-y^2/2} f(y) = (\omega\tau)^{\frac{1+i\omega\tau}{2}} \int_0^\infty dx e^{-\omega\tau(x^2/2 - i \log(x))} f(x\sqrt{\omega\tau}) \quad (30)$$

need to be evaluated. Extremizing the argument of the exponential $\Psi = \omega\tau(x^2/2 - i \log(x))$ in the second form of the integral gives the saddle point at $z^* = (1 + i)/\sqrt{2}$. Like for the

shot-noise case, the integral is deformed onto the complex plane to run through the saddle point, from the origin to the point $z = 0 + i/\sqrt{2}$ and then from that point to $z = \infty + i/\sqrt{2}$. Hence the ratio of integrals can be written

$$\frac{I_f}{I_g} = \frac{i \int_0^\infty da e^{-\Delta\Psi(ia)} f(a\sqrt{i\omega\tau}) + \int_0^\infty db e^{-\Delta\Psi(b+i/\sqrt{2})} f((b+i/\sqrt{2})\sqrt{\omega\tau})}{i \int_0^\infty da e^{-\Delta\Psi(ia)} g(a\sqrt{i\omega\tau}) + \int_0^\infty db e^{-\Delta\Psi(b+i/\sqrt{2})} g((b+i/\sqrt{2})\sqrt{\omega\tau})} \quad (31)$$

where $\Delta\Psi(x) = \Psi(x) - \Psi(z^*)$.

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