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# Modeling of time domain diffuse Raman spectroscopy in a two-layer medium

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## ABSTRACT

A model, based on the solution of two coupled diffusion equations to the excitation and emission wavelengths, respectively, was developed to describe the Raman signal in the time domain in a reflectance configuration in a two-layer medium. The accuracy of the model is characterized by comparison with the results of Monte Carlo simulations. This solver can correctly account for the Raman emitters within the layers and the full wavelength dependence of the optical properties of the layers. The short computation time of this solver makes it suitable for use in reconstructing Raman spectra from time domain measurements at multiple wavelengths.

**Keywords:** Diffuse optics, Diffusion equation, Raman Scattering, Raman spectra, Monte Carlo simulations

## 1. INTRODUCTION

Time-Domain Diffuse Raman Spectroscopy<sup>1-5</sup> is a recent technique that combines Time-Domain Diffuse Optics with Raman Spectroscopy, and it offers the possibility to keep together the advantages of both techniques,<sup>3</sup> that is the possibility to get information deeply from the medium and to unveil hidden information on its chemical composition. The development of time-domain diffuse Raman spectroscopy is conditional on the availability of a model capable of describing photon migration in the media of interest. Thus, the correct modeling of light propagation through the medium is a fundamental information at the basis of this technique for a correct retrieval of the Raman spectra from the investigated medium.<sup>5,6</sup> Time domain spontaneous Raman scattering in highly diffusive media involves three main approaches: stochastic forward solvers based on Monte Carlo simulations,<sup>6-8</sup> analytical heuristic solutions of the Raman interactions<sup>5,7,8</sup> and analytical rigorous solutions of diffusion equation (DE).<sup>5,7,8</sup> Although Monte Carlo (MC) simulations can be performed for any type of geometry, they are computationally expensive and their use for the inverse problem is very limited. In contrast, exact analytical forward solvers are significantly faster, however their availability is limited to homogeneous geometries.<sup>6-8</sup> In this work, the photon migration of the Raman signal through a two-layer medium is addressed with both Monte Carlo simulations and with a heuristic model offer significant advantages compared to the existing ones.<sup>5</sup> The Monte Carlo results are used as a reference for the verification of the analytical model.

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## 2. THEORY

In general, as shown in previous works, the Raman solution across any geometry using the DE can be written using two coupled DEs, one at the excitation wavelength ( $\lambda$ ), and one at the emission wavelength ( $\lambda_e$ ),<sup>6-8</sup> and from now on, the quantities without suffix are related to the excitation wavelength, and the quantities with the suffix  $e$  pertain to the emission wavelength. The geometry considered is a two-layer cylinder of radius  $L$  and thicknesses  $s_1$  and  $s_2$  for the first and second layer, respectively. Pertaining to  $\lambda$ , we denote by  $\mu_{a1}$  and  $\mu_{a2}$  the absorption coefficients of first and second layer, by  $\mu'_{s1}$  and  $\mu'_{s2}$  the reduced scattering coefficients of first and second layer, by  $\mu_{sR1}$  and  $\mu_{sR2}$  the Raman scattering coefficients of first and second layer, and by  $n_1$  and  $n_2$  the refractive indices in first and second layer. Similarly, the symbols  $\mu_{a1e}$ ,  $\mu_{a2e}$ ,  $\mu'_{s1e}$ ,  $\mu'_{s2e}$ ,  $n_{1e}$  and  $n_{2e}$  are referred to the same quantities at  $\lambda_e$ . It is important to note that the modeling implemented here of Raman scattering follows the same frame described in previous works.<sup>6,8</sup>

Modeling the time-domain Raman fluence signal implies the calculation of the following integral:<sup>6,8</sup>

$$\Phi_{Raman}(\vec{r}, t) = \int_0^t \int_{V'} \mu_{sR}(\vec{r}') \Phi_G(\vec{r}_s, \vec{r}', \dots, t') \Phi_{Ge}(\vec{r}', \vec{r}, \dots, t - t') d\vec{r}' dt', \quad (1)$$

where  $\Phi_G$  is the Green's function for the two-layer medium at  $\lambda$  and  $\Phi_{Ge}$  the same Green function at  $\lambda_e$ . The symbol  $V'$  denotes the volume of the two-layer medium. The solution of Eq. (1) is obtained assuming that only single-scattering Raman event contribute to the signal. The solving of this integral is computationally burdensome with the risk of obtaining a model whose calculation is not fast enough. For this reason, we have opted to approach heuristically this calculation.

The realization of the heuristic model stems from some observations made on the comparison of the temporal point spread functions (TPSFs) for the layered medium and the TPSFs for the homogeneous medium with given values of the optical properties of the first and second layer. We can expect that the Raman signal emitted by this two-layer medium to be composed of two parts: one part from the Raman emission of the first layer and one part from the Raman emission of the second layer. Following this logic, we can imagine the Raman signal emitted by the two-layer medium expressed heuristically as follows:

$$\Phi_{Raman}(\vec{r}, t) = c_1(t) \Phi_{1Raman}(\vec{r}, t) + c_2(t) \Phi_{2Raman}(\vec{r}, t), \quad (2)$$

where  $\Phi_{1Raman}(\vec{r}, t)$  and  $\Phi_{2Raman}(\vec{r}, t)$  are two Raman solutions for the Raman signal obtained solving the DE in equivalent homogeneous media determined by considering constant optical properties equal to those of the first and second layer, respectively. These kinds of solutions, based on the extrapolated boundary condition,<sup>7-9</sup> for a cylinder geometry and for a parallelepiped can be found in the previous literature.<sup>6,8</sup> While  $c_1(t)$  and  $c_2(t)$  are coefficients, to be determined, that express the relative weight of the two terms, and it is reasonable to expect them to be quantities proportional to the path spent in the respective layers by the photons received at time  $t$ . We can therefore define these coefficients as:<sup>5,8</sup>

$$c_1(t) = \frac{\langle l_1 \rangle(t)}{\langle l_1 \rangle(t) + \langle l_2 \rangle(t)}, \quad c_2(t) = \frac{\langle l_2 \rangle(t)}{\langle l_1 \rangle(t) + \langle l_2 \rangle(t)}, \quad (3)$$

where  $\langle l_1 \rangle(t)$  and  $\langle l_2 \rangle(t)$  are the average paths spent, in the two-layers of the medium, by the photons received at the detector site  $\vec{r}$  at time  $t$ . Recall that these quantities can be calculated by the analytical solution for the fluence of the DE in a two-layer medium,  $\Phi_{2layers}(\vec{r}, t)$ , considering light propagating at the excitation wavelength.<sup>5,8</sup> We thus have that:

$$\langle l_1 \rangle(t) = -\frac{1}{\Phi_{2layers}(\vec{r}, t)} \frac{\partial \Phi_{2layers}(\vec{r}, t)}{\partial \mu_{a1}}, \quad \langle l_2 \rangle(t) = -\frac{1}{\Phi_{2layers}(\vec{r}, t)} \frac{\partial \Phi_{2layers}(\vec{r}, t)}{\partial \mu_{a2}}. \quad (4)$$

Since the analytical solutions for  $\Phi_{2layers}$  (two-layer medium) and for  $\Phi_{1Raman}$  and  $\Phi_{2Raman}$  (homogeneous medium), are available,<sup>6-8</sup> the model can thus be calculated. It is worth to note that for the limit cases  $s_1 = 0$  and  $s_1 = \infty$  the model is exact within the diffusion approximation since in these cases it is simply the exact DE solution for the time-domain Raman signal in a homogenous medium already described in previous works.<sup>6,8</sup>

Making use of Eq. (2) the time-domain Raman signal received in reflectance configuration from the two-layer medium illuminated by a pulse source can be obtained by using Fick's law (see Fig. 1) as

$$R_{Raman}(\rho, t) = D \frac{\partial}{\partial z} \Phi_{Raman}(\rho, z = 0, t), \quad (5)$$

or, alternatively, by using the extrapolated boundary partial current condition as<sup>7,8</sup>

$$R_{Raman}(\rho, t) = \frac{\Phi_{Raman}(\rho, z = 0, t)}{2A}, \quad (6)$$

with  $A$  a coefficient related to Fresnel reflection coefficient depending on the refractive index mismatch between medium and external.<sup>7-9</sup>

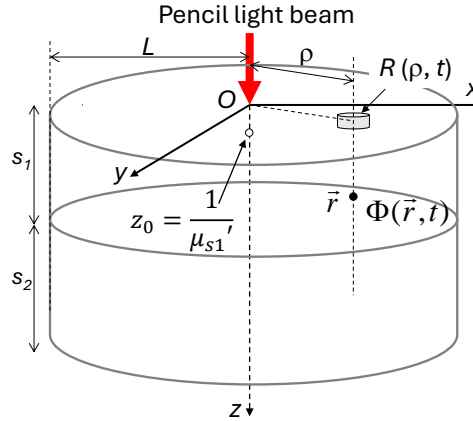


Figure 1. Schematic of a two-layer cylinder.

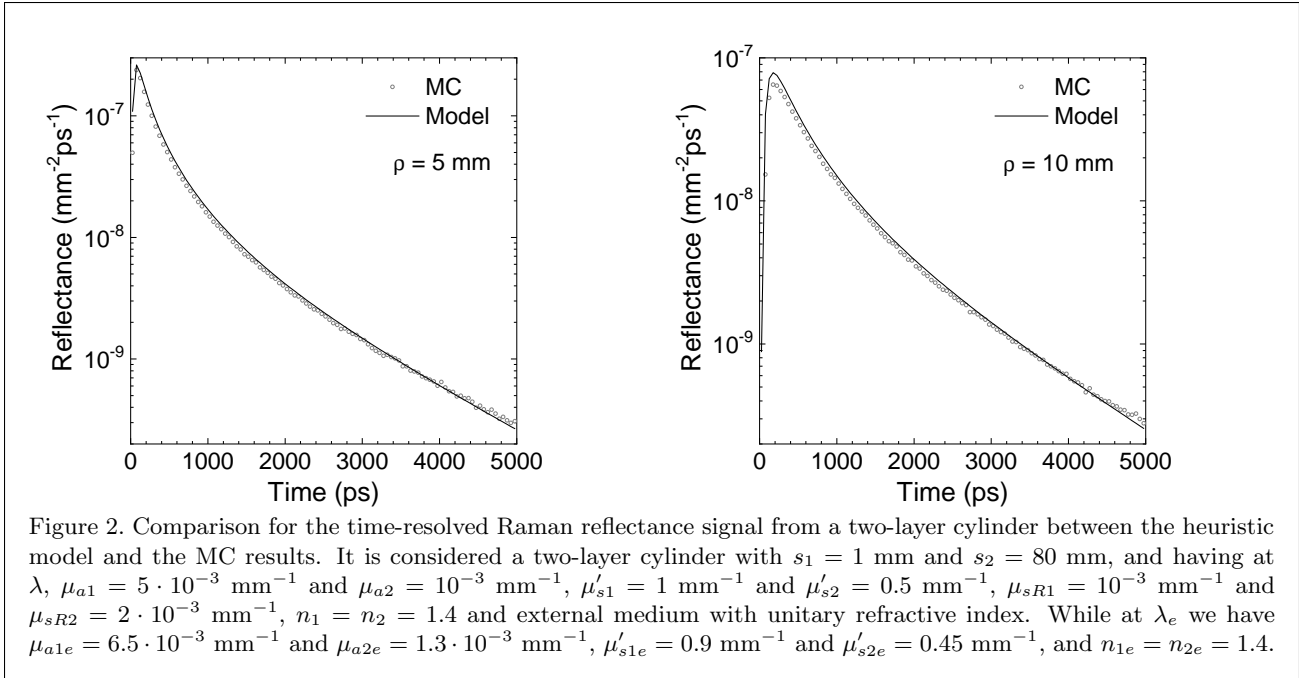
The computation time of this forward solver is mainly determined by the computation time of the two-layer model necessary for the calculation of  $\langle l_1 \rangle(t)$  and  $\langle l_2 \rangle(t)$  and it is compatible to the use of the solver in inverse procedures.

### 3. RESULTS

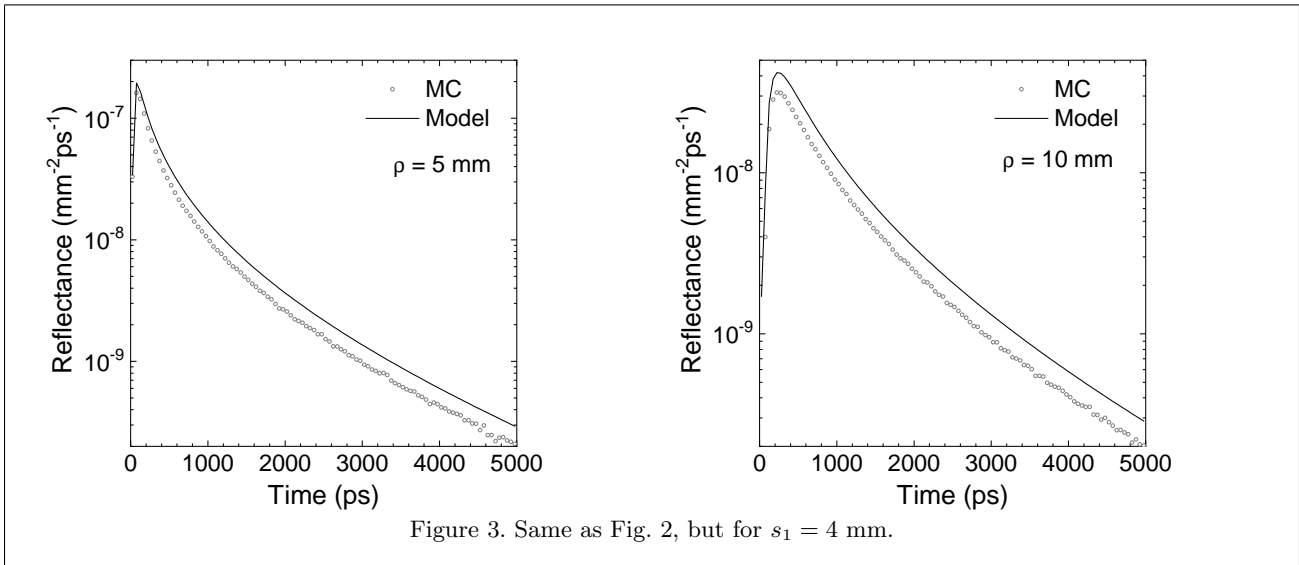
The results obtained with the heuristic model were preliminarily compared with the the results of MC simulations. The MC results have been obtained by extending a previously developed code for simulating Raman propagation through an homogeneous medium to the case of a two-layer geometry.<sup>6</sup>

#### 3.1 Comparisons between the heuristic model and Monte Carlo simulations

The results of the heuristic solution of Eq. (2) with the reflectance calculated by means Eq. (6) are calculated and compared to MC results. Similar results were obtained by calculating the reflectance with Eq. (5). It is considered a two-layer cylinder where a pencil light beam is imping at the center of the entrance surface (Fig. 1). In the analytical heuristic model the pencil beam is modeled by inserting an isotropic unitary pulse  $\varepsilon(\vec{r}, t) = \delta(\vec{r} - \vec{r}_s)\delta(t)$  at a transport mean free path, i.e.,  $\vec{r}_s = (0, 0, z_0 = 1/\mu'_{s1})$ .<sup>7-9</sup> It is considered a two-layer cylinder having at  $\lambda$ ,  $\mu_{a1} = 5 \cdot 10^{-3} \text{ mm}^{-1}$  and  $\mu_{a2} = 10^{-3} \text{ mm}^{-1}$ ,  $\mu'_{s1} = 1 \text{ mm}^{-1}$  and  $\mu'_{s2} = 0.5 \text{ mm}^{-1}$ ,  $\mu_{sR1} = 10^{-3} \text{ mm}^{-1}$  and  $\mu_{sR2} = 2 \cdot 10^{-3} \text{ mm}^{-1}$ ,  $n_1 = n_2 = 1.4$  and external medium with unitary refractive index. While at  $\lambda_e$  we have  $\mu_{a1e} = 6.5 \cdot 10^{-3} \text{ mm}^{-1}$  and  $\mu_{a2e} = 1.3 \cdot 10^{-3} \text{ mm}^{-1}$ ,  $\mu'_{s1e} = 0.9 \text{ mm}^{-1}$  and  $\mu'_{s2e} = 0.45 \text{ mm}^{-1}$ , and  $n_{1e} = n_{2e} = 1.4$ . The cylinders considered had  $s_2 = 80 \text{ mm}$ , and  $s_1 \in \{1, 4\} \text{ mm}$  with a radius  $L$  of  $100 \text{ mm}$ . Figure 2 shows two examples of results for  $s_1 = 1 \text{ mm}$ , while Fig. 3 pertains to  $s_1 = 4 \text{ mm}$ . The figures compare the results for the Raman time-resolved signal to the MC simulations for two source-detector distances:  $\rho \in \{5, 10\} \text{ mm}$ . The comparisons of Fig. 2 show that for very small value of the first



layer thickness the prediction of the heuristic model tend to be exact within the validity of the DE. For the larger thickness of the first layer considered in Fig. 3 we note larger differences between heuristic model and MC simulations; however, the model, while showing appreciable differences in the amplitude of the temporal profile, almost correctly reproduces the shape of the time-resolved reflectance, especially at short and late times, when the first and second layers contribute predominantly, respectively. This fact it is very important for the future use of the model in time-domain Raman spectroscopy for which the shape of the profile is providing the relevant information for retrieving the desired targets of the technique. Thus, although the heuristic structure of the model that compromise the information on the amplitude, the model is able to return the main dependence of the shape of the profile from the optical properties of the two layers at both excitation and emission wavelength.



## 4. CONCLUSIONS

In this contribution, we have developed a heuristic model for describing the time-domain Raman signal from a two-layer medium that can account the full dependence of the signal from the optical properties of the layers at both excitation and emission wavelength. Thus, compared to previous works,<sup>5,10</sup> we introduced the possibility of having a model capable of accounting for the dependence of the Raman signal on the optical properties of the layers at the emission wavelength, which had been omitted in the previous contributions. The heuristic nature of the model brings some deficiencies in reproducing the time-resolved Raman signal, mainly in the amplitude. However, the improvement over the previous model is significant and we expect it to result in a significant improvement in reconstructing Raman spectra of two-layer diffusive media from time-resolved, multi-wavelength Raman signals acquired in reflectance configuration.<sup>5,10</sup>

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## REFERENCES

- [1] Matousek, P., Clark, I. P., Draper, E. R. C., Morris, M. D., Goodship, A. E., Everall, N., Towrie, M., Finney, W. F., and Parker, A. W., "Subsurface Probing in Diffusely Scattering Media Using Spatially Offset Raman Spectroscopy," *Appl. Spectrosc.* **59**, 393–400 (Apr 2005).
- [2] Hooijschuur, J. H., Iping Petterson, I. E., Davies, G. R., Gooijer, C., and Ariese, F., "Time resolved Raman spectroscopy for depth analysis of multi-layered mineral samples," *Journal of Raman Spectroscopy* **44**(11), 1540–1547 (2013).
- [3] Sekar, S. K. V., Mosca, S., Tannert, S., Valentini, G., Martelli, F., Binzoni, T., Prokazov, Y., Turbin, E., Zschratte, W., Erdmann, R., and Pifferi, A., "Time domain diffuse raman spectrometer based on a tcspc camera for the depth analysis of diffusive media," *Opt. Lett.* **43**, 2134–2137 (May 2018).
- [4] Bossi, A., Sekar, S. K. V., Lacerenza, M., Lacerenza, M., Gandolfi, V., Šušnjar, S., Lanka, P., D'Andrea, C., Vanna, R., Valentini, G., Farina, A., and Pifferi, A., "Time domain diffuse raman spectroscopy using single pixel detection," *Biomedical Optics Express* **14**, 11.
- [5] Šušnjar, S., Martelli, F., Mosca, S., Sekar, S. K. V., Swartling, J., Reistad, N., Farina, A., and Pifferi, A., "Two-layer reconstruction of raman spectra in diffusive media based on an analytical model in the time domain," *Opt. Express* **31**, 40573–40591 (Nov 2023).
- [6] Martelli, F., Binzoni, T., Sekar, S. K. V., Farina, A., Cavalieri, S., and Pifferi, A., "Time-domain raman analytical forward solvers," *Optics Express* **24**, 20382–20399 (9 2016).
- [7] Martelli, F., Del Bianco, S., Ismaelli, A., and Zaccanti, G., [*Light propagation through biological tissue and other diffusive media: theory, solutions, and software*], SPIE (2009).
- [8] Martelli, F., Binzoni, T., Del Bianco, S., Liemert, A., and Kienle, A., [*Light propagation through biological tissue and other diffusive media: theory, solutions, and validations*], SPIE press Bellingham, Washington (2022).
- [9] Contini, D., Martelli, F., and Zaccanti, G., "Photon migration through a turbid slab described by a model based on diffusion approximation. I. Theory," *Applied Optics* **36**(19), 4587–4599 (1997).
- [10] Šušnjar, S., Martelli, F., Swartling, J., Reistad, N., and Pifferi, A., "Reconstruction of Raman spectra of two-layer diffusive media: model-based approach in time-domain," in [*Diffuse Optical Spectroscopy and Imaging IX*], Contini, D., Hoshi, Y., and O'Sullivan, T. D., eds., **12628**, 126280R, International Society for Optics and Photonics, SPIE (2023).