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COMPARATIVE STUDIES FOR MULTIVARIATE MODEL OF HUMAN BLOOD TISSUE USING GAUSSIAN AND LORENTZ OSCILLATORS AND ANALYSIS USING PLS REGRESSION

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ABSTRACT

The paper presents the modeling of the Multivariate model of the Human blood tissue using Gaussian and Lorentz Oscillators. The authors have demonstrated the spectroscopic modeling of the tissue in the region of near infrared i.e 2000nm to 2500 nm, using the concept of fundamental oscillators responsible for the energy of the composition under study. Usually the two approaches i.e. Gaussian and Lorentz are very popular of which later is complex for modeling the system as it required additional parameter i.e. number of oscillators, Line width of Oscillators and Strength of each oscillator. The general model is customized for the human tissue consisting of five major constituents i.e. serum Alanine, serum urea, HDL Lactate and Ascorbate and Glucose in the physiological concentration in the human tissue. Here the ensemble of around 1000 spectra's were generated for the template in the physiological concentration of normal population. The Partial Least Square Regression studies were performed for the both the approached for validation model with RMSE and Clark Error Grid analysis.

KEYWORDS: Multivariate, Lorentz, Gaussian, Glucose, PLSR

INTRODUCTION

Near-infrared (NIR) spectroscopy has increasingly been adopted as an analytical tool in various fields, such as the petrochemical, pharmaceutical, environmental, clinical, agricultural, food and biomedical sectors during the past 15 years. In recent years, near-infrared (NIR) spectroscopy has gained wide acceptance in different fields by virtue of its advantages over other analytical techniques, the most salient of which is its ability to record spectra for solid and liquid samples without any pretreatment[1]. NIR spectroscopy offers several advantages over mid-IR (mid-infrared) spectroscopy in a non-invasive glucose monitoring system, e.g. less background interference due to water absorption, and penetration depths are greater at the shorter wavelengths, which is necessary for monitoring blood glucose in capillaries and glucose in interstitial fluid and tissue [2]. NIR spectroscopy also offers advantages over Raman spectroscopy , such as (i) higher SNRs, (ii) a broad-band light source is used instead of the highly monochromatic source necessary for Raman spectroscopy, and (iii) because the Raman effect is exceedingly weak (i.e., very low SNRs) the detector is usually cooled by either liquid nitrogen or thermoelectrically cooled, which is not necessary in NIR spectroscopy[3]. Disadvantages of using NIR spectroscopy include the following: (i) NIR spectra are usually relatively featureless as compared to mid-IR spectra and (ii) combination bands and overtones are predominant in the NIR region for biological substances. Application of NIR spectroscopy for Biomedical field is not much explored hence we have decided to use the NIR range to estimate the glucose level in human blood. We have decided to simulate the spectra's of human blood using matlab 7. The main reason behind the simulating

human blood spectra in NIR region is difficult to carry out the infrared spectroscopy experiments for the hygroscopic sample due to the unavailability of the sample holders. The sample holder like KBr , NaCl and *CaF2* are soluble in water which cannot be used to perform the experiments of the laboratory sample, which needs to be carried out for calibrating the model to find out the concentration of glucose in blood. Secondly the available ZnSe holders are very costly and are not available easily.

HUMAN BLOOD SPECTRA SIMULATION USING LORENTZ AND GAUSSIAN OSCILLATOR APPROACH

The absorption spectrum of human blood depends on the type of predominant absorption center and water content of tissue. Absolute value of absorption coefficients for typical tissue lie in the range of 10^{-2} to 10^{14} cm^{-1} [4]-[7]. Glucose is one of the most important carbohydrate nutrient sources and is fundamental to almost all biological processes. Quantification of glucose concentration is important in monitoring and analysis of control and regulation of cell culture, and diagnosis and control of human disease including diabetes. The near-infrared (NIR) region of the optical spectrum extend from 700nm – 2500 nm which is used for quantitative measurement of organic functional groups , specially C-H, O-H, N-H, and C=O. The absorption bands in the NIR are composed primarily of overtones and combination bands of stretching and vibrational modes of organic molecules. Major five constituents interfering with glucose in the region of 2000-2500nm are serum Alanine, serum urea, HDL Lactate, Glucose , Ascorbate interfere with the whole blood glucose to generate a complex signature in the spectrum region[18]. Also the tissue temperature and skin complexion due to pigment variation over the globe population has influence on the transmission characteristics. There are many other factor influencing the signature of a spectrum, but the analysis becomes complex as the physiology of the body is very sensitive and dynamic over the catabolic processes involved. It has been decided to model this complex ensemble over various concentrations of five chemical constituents and two physical components namely skin complexion and the body temperature [8]-[17]. There are basically two methods to model any desired spectra 1) Lorentz oscillator 2) Gaussian Oscillator.

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{K/\mu} \tag{1}$$

Resonance Frequency : 'K' is the force constant, μ=m1m2/(m1-m2) is the reduced mass , typical atomic masses are 1, 12, and 16 and bond strengths are 8. 5, 4.5 and 16 N/cm. Therefore, resonant frequencies is in the NIR part of the electromagnetic spectrum from 2 ~ 20 um

Multivariate Model Using Lorentz Oscillators

We have generated required generalized response and predictor matrix using Lorentz Oscillator Eq. 2, with respective oscillator strength, width and central frequency. The flow chart for spectra generation in region of interest is given in Figure 1.

$$(n + i.k) = \left(\varepsilon_{\infty} + \sum_{j} \frac{S_j \nu^{2}{}_{j}}{\nu^{2}{}_{j} - \nu^{2} - i\nu\Gamma_j} \right)^{1/2} \tag{2}$$

Where 'n' →response of spectrum

'i.k' → imaginary components of the frequency response;

'Sj' →strengths of the oscillators

'vj' →central frequency;

'Γj' →width of oscillator

'ε_∞'→represents the electronic contribution to the complex dielectric constant.

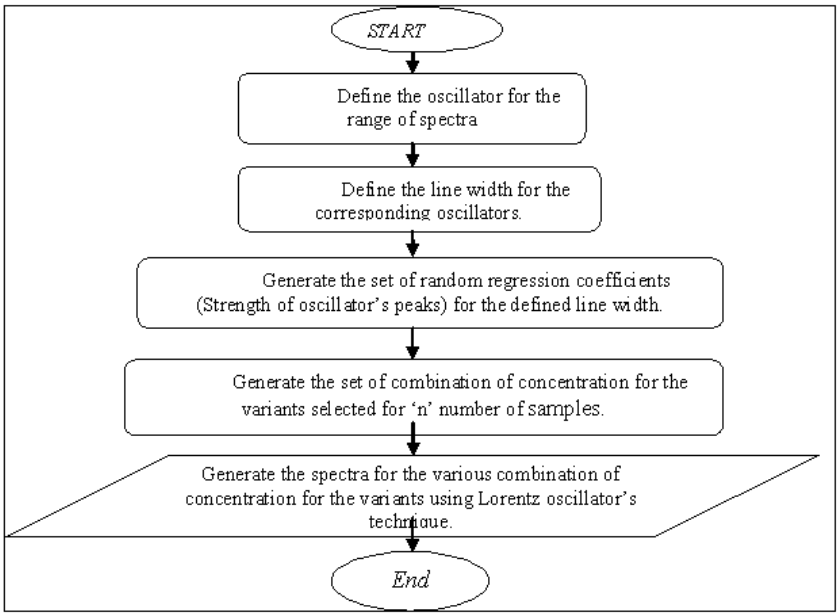

Figure 1: Flow Chart of the Simulated Spectra Generated by Lorentz Oscillator Model

Table 1: Various Oscillators Parameters used in the Lorentz Expression

Variants	Oscillator Number	1	2	3	4	5
Alanine	CF	2130	2242	2295	2320	2530
	OW	150	25	30	30	50
	SO	230	30	20	51	40
Urea	CF	2080	2150	2200	2240	2550
	OW	40	50	50	140	250
	SO	1	3	10	16	12
HDL Lactate	CF	2050	2150	2198	2258	2350
	OW	150	100	80	40	80
	SO	1.5	10	10	10	12
Glucose	CF	2100	2150	2250	2320	2480
	OW	100	100	60	60	100
	SO	1.4	0.6	0.5	0.5	0.6
Ascorbate	CF	2125	2160	2280	2340	2490
	OW	70	100	60	100	50
	SO	48	90	30	40	40

CF: Centre frequency; OW Oscillator width; OS Oscillator strength

The whole blood spectrum model for various concentrations of the five variants has been generated. The model considered the following values of concentration for the human blood chemometrics system well within the pathological range. The concentrations of the five constituents were; C1=Alanine (1-21gm/dl), C2=Serum Urea (7-18 gm/dl), C3=HDL Lactate (4.5-14.4mgm/dl), C4= Glucose (70-110 mg/dl), C5=Ascorbate (0.4-1.5gm/dl) and other two physical parameters were C6=temperature(25-40 ^{0}C), C7=skin complexion (0.2 - 0.4). Oscillators' parameters as shown in Table 1 were used to generate the signature of the five chromospheres as shown in Figure 2.

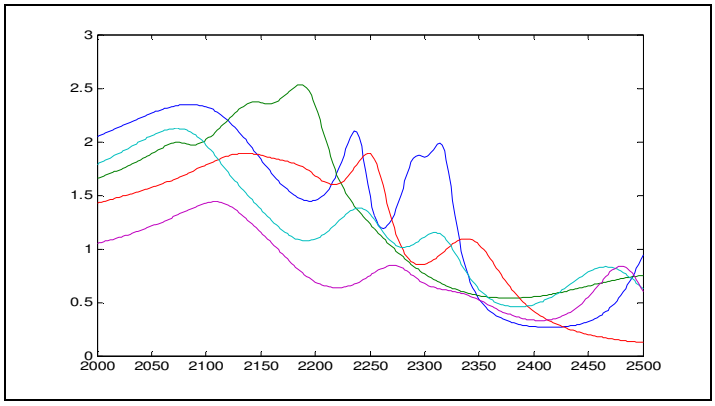

Figure 2: Signature of Five Major Components Simulated using Lorentz Oscillators

The Lorentz model is so flexible that just by varying the strength, line width and natural frequency any practical spectrum can be generated with highly non-linear behavior. The unknown spectrum within the confidence interval of the calibrated spectra can be generated adopting same principle that of calibration spectral as shown in flow chart (Figure 1).

The resultant spectra of all blood constituents in the range 2000nm -2500nm will have the form shown in Figure 3. Samples Template where generated for different combinations of blood constituents as shown in Figure 4.

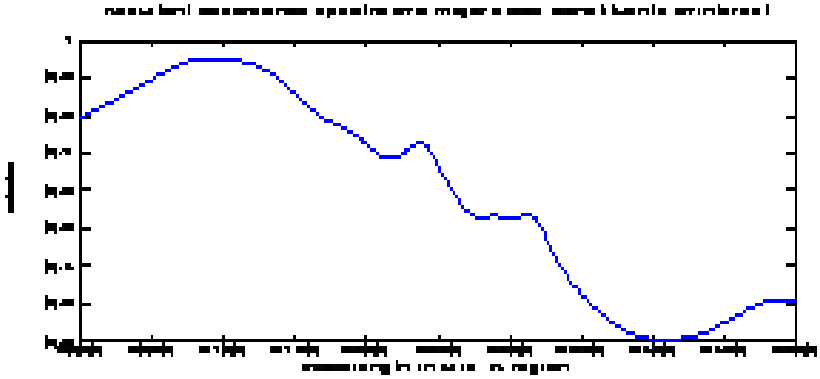

Figure 3: Resultant Normalized Signature of Various Components Simulated Using Lorentz Oscillator

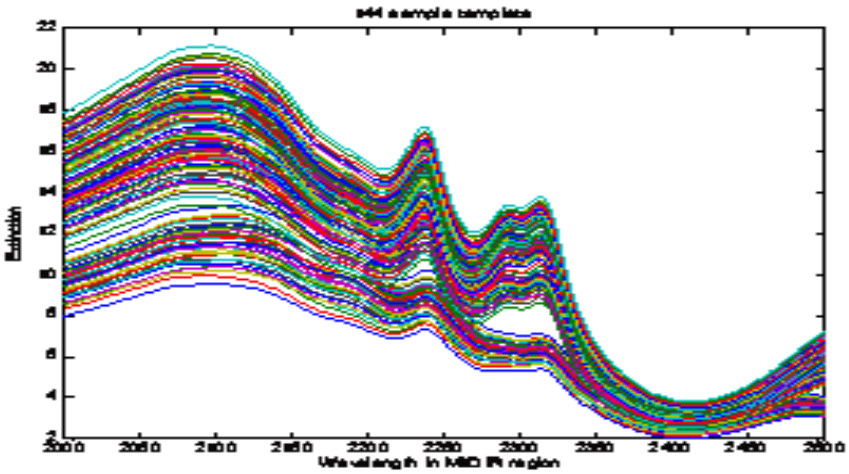

Figure 4: 1024 Samples Template for the PLSR Model Generated Using Lorentz Oscillator

Multivariate Model Using Gaussian Oscillators

Gaussian function has the form as given in the Eq. (3), which can be extended to generate the required spectra with superposition multiple oscillators at respective frequencies.

$$f(x) = ae^{-\frac{(x-b)^2}{2c^2}} \tag{3}$$

Where $a = 1/(\sigma\sqrt{(2\pi)})$, $b = \mu$, $c = \sigma$, *some real constants a, b, c > 0, and* $e \approx 2.718281828$,

The strength and energy spread of the oscillator is decided by the parameneter σ and central frequency oscillator by μ. The Gaussian model is so user friendly in tuning the respective spectra's just by varying 2 parameters μ, σ. We have generated the 1024 templates whose behavior is shown in figure 5. The oscillator parameters are shown in table 2.In order to simulate the blood tissue spectra using Gaussian approach we require only two parameters one is μ and other is σ. The value of σ required is very small compared to the Lorentz to get the same spectra.

Table 2: Various Oscillators Parameters used in the Gaussian Expression

Variants	Oscillator Number	1	2	3	4	5
Alanine	μ	2130	2242	2295	2320	2530
	σ	0.4	0.2	0.13	0.065	0.2
Urea	μ	2080	2150	2200	2240	2550
	σ	0.39	0.32	0.14	0.08	0.13
HDL Lactate	μ	2050	2150	2198	2258	2350
	σ	19	23	26	40	16
Glucose	μ	2100	2150	2250	2320	2480
	σ	2	0.6	0.8	0.18	0.2
Ascorbate	μ	2125	2160	2280	2340	2490
	σ	1	0.8	0.3	0.3	0.23

μ: Centre frequency; σ: Oscillator width; Oscillator strength

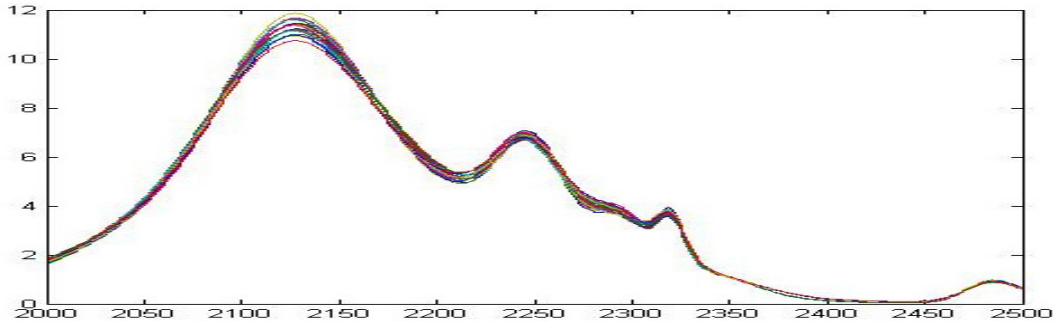

Figure 5: 1024 Samples Template for the PLSR Model Generated Using Gaussian Oscillator

RESULTS AND DISCUSSIONS

Multivariate Analysis on simulated blood spectra's:

Multivariate PLSR analysis is performed on the data sets generated by Lorentz and Guassian method. A Root mean square error RMSE analysis was performed over the prediction of the variants concentrations.

The RMSE analysis for the lorentzian based generated spectra is 3.459 for Glucose [19]. The RMSE analysis for the Gaussian based generated spectra is 0.0 for Glucose and other variants except for Ascorbate (shown in table 3).

Table 3: RMSE Analysis

C1	C2	C3	C4	C5	C1 Pre	C2 Pre	C3 Pre	C4 Pre	C5 Pre
15	10	5	70	1	15	10	10	70	1.2
15	10	5	90	0.5	15	10	10	90	0.8
15	10	10	70	0.5	15	10	15	70	0.7
15	15	5	90	0.5	15	15	10	90	0.8
20	10	5	70	0.5	20	10	10	70	0.7

C1: Alaline C2:Urea C3:Lactate C4:Glucose C5: Ascorbate

We have selected the 5 templates among 1024 as unknown and the same temples are then passed through PLSR model to predict the unknown variants concentration. The predicted values are same as that of actual concentration of the variant.

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