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## Floating reference position-based correction method for near-infrared spectroscopy in long-term glucose concentration monitoring

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**Abstract.** We present a floating reference position (FRP)-based drift correction method for near-infrared (NIR) spectroscopy-based long-term blood glucose concentration (BGC) monitoring. Previously, we reported that it is difficult to quantify the systematic drift caused by the fluctuation of incident light intensity at different source-detector (SD) separations based on the absolute FRP change. We use the relative FRP change as a baseline reference to quantitatively characterize the signal drift at different SD separations. For the wavelengths that were used, a uniform equation was developed to describe the relationship between the drift and the relative FRP change. With the help of this equation, the correction can easily be performed by subtracting the systematic drift estimated by the equation. A theoretical analysis and an experimental phantom study demonstrated that our method could be used for systematic drift correction in NIR spectroscopy for long-term BGC monitoring. Moreover, the analysis method can also be referenced to reduce drifts from multiple sources. © 2017 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JBO.22.7.077001]

Keywords: near-infrared spectroscopy; drift correction; scattering medium; blood glucose; floating reference position; noninvasive measurement.

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#### 1 Introduction

Near-infrared (NIR) spectroscopy is one of the most promising methods for noninvasive blood glucose concentration (BGC) measurement.<sup>1-3</sup> However, its application in long-term in vivo BGC monitoring remains a challenge due to unsatisfactory accuracy.<sup>4-6</sup> The established spectral prediction model based on BGC values measured using the oral glucose tolerance test method is commonly considered "time-limited" because it would not be available after a day.<sup>4-6</sup> Generally, background disturbances during long-term monitoring, which may involve instrument drift, change of surrounding temperature, variations of man-machine interfaces, physiological fluctuation in the body, etc., would markedly change the spectra and lead to an unacceptable deviation for predicted BGC values.<sup>3,7</sup> Except for unavoidable disturbances caused by physiological fluctuation, the other disturbances related to instrument or manmachine interfaces should be well controlled and reduced. Some advanced devices with reference optical paths were applied with the goal of eliminating the drift of signals from instruments.<sup>8,9</sup> Some probes designed with attached sensors have also been applied because they can precisely monitor the location on the skin and reproduce the skin contact for repeated tests.<sup>10</sup> However, there is still random fluctuation of incident light intensity in these cases because the incident angle or the surface reflectance of light varies randomly. We are planning to develop an effective mathematical correction method to try to greatly reduce the drift related to varying incident light intensities, which may be caused by the randomly varying skin-probe contact or drift of the light source.

Our correction is based on using a reference signal from the subject itself, and the reference is considered a good index for monitoring the variations related to skin-probe contact as well as the physiological skin conditions.<sup>11</sup> This reference-based correction and the subsequent measurements might yield higher accuracy in long-term BGC monitoring.<sup>12</sup> This correction approach (VRCA). Moreover, the reference can be set in various ways, such as a time-based,<sup>13</sup> position-based,<sup>13</sup> or wavelength-based reference.<sup>14</sup>

In recent years, a position-based VRCA has been considered promising in BGC measurements because it can provide satisfactory glucose absorption information with a sufficiently long equivalent optical path length.<sup>15,16</sup> In addition, the introduction of a floating reference position (FRP), which involves a special source-detector (SD) separation, has been identified as an excellent position reference. At an FRP, the change in diffuse reflection of the light intensity signal caused by disturbances can be directly monitored because it is sensitive to disturbances but insensitive to BGC variations.<sup>16-19</sup> However, the correction using FRP is also challenging because the drifts from different positions, i.e., SD separations, are completely different from their reference, the FRP. The relationship between the drifts from the focused SD separations and the FRP should first be determined. Zhang<sup>19</sup> estimated the ratios between the drifts from the FRP and two other SD separations when the drifts occurred as the light source was set on different output powers, and then the correction was performed using the ratios. However, the empirical ratios are only available for the two

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SD separations and wavelengths used. It is difficult to reference other SD separations and wavelengths.

In this paper, we report that the relative changes in diffuse reflection intensity are approximately linear with SD separations when either the incident light intensity or glucose concentration varies. In previous investigations, the absolute changes in diffuse reflection intensity from different SD separations were considered totally different and exponential-like. After using the relative approach, we recognized that the linearity of the drift could be a very helpful indicator of the relationship between the variations from different positions including the FRP. We could even estimate all possible values of the relative change of diffuse light intensity for all positions by performing spectral data recording at only a few positions. Furthermore, we found that the relative changes seem to be similar for the different positions where only incident light intensity varies. Therefore, the ratio between the drifts from different SD separations and FRP can be easily acquired using an equation we developed. The correction can easily be performed for all wavelengths from 1100 to 1400 nm as well as for SD separations.

#### 2 Materials and Methods

#### 2.1 Experimental System

A supercontinuum source (SC46, YSL photonics, China) with a broadband from 600 to 1700 nm is used as light source in the custom-built NIR spectrometer. As shown in Fig. 1, the system is equipped with a noncollinear acousto-optic tunable filter (TEAF10-1.0-1.8-S, Brimrose Company, Maryland) as the light splitting element to provide a spectral response range from 1100 to 1400 nm (9091 to 7143 cm<sup>-1</sup>) with a resolution of 2 nm, an InGaAs infrared detector (G12181-210K, Hamamatsu Photonics K.K., Japan), and a 16-bit data acquisition board (PCI-6220, National Instrument Inc.). The fiber used in the experiment is multimode fiber, its core diameter is 200  $\mu$ m, and its numerical aperture is 0.22.

#### 2.2 Samples

NIR diffuse reflection spectra were recorded for the scattering media of 10% Intralipid solution<sup>20,21</sup> with different glucose concentrations, which are from 0 to 2000 mg/dL with an interval of 200 mg/dL.

#### 2.3 Measurements

Twenty-two detection distances of SD separations were set from 0.47 to 3.095 mm with an interval of 0.125 mm. The



Fig. 1 Schematic illustration of the measurement system.

surrounding temperature was controlled at 25°C. All samples were measured 5 times within 48 h, and the samples were tested in a random order every time. The samples were placed on a magnetic plate and stirred for 1 min and then allowed to settle for 3 min before recording. The test time was arranged to start at 9:16 am and 9:16 pm of the first day, 9:15 am and 9:15 pm of the second day, and 9:16 am of the third day. We call the five times tests first, second, third, fourth, fifth tests, respectively. Measuring all SD separations and wavelengths for one sample took ~50 s and all 11 samples took 10 min.

Every separate test from the five tests can be considered as a short-term test, where the R' can demonstrate  $R'_{G}$  caused by glucose. But between the five tests, which lasted for 48 h, the R' for a same sample can demonstrate  $R'_{D}$  caused by light source drift.

#### 2.4 Defining Relative Changes in Diffuse Reflection Light Intensity

Figure 2 shows the diffused light in a scattering medium, where  $I_0$  is the incident light intensity, and I is the diffuse reflection light intensity.

The relative variation of diffuse reflection light is defined as R' in Eq. (1), where I is the diffuse reflection light intensity and  $\Delta I$  is the variation of I as referenced to an initial state of the scattering medium.  $I_r$  denotes the diffuse light intensity for reference.  $\Delta I$  can be induced by glucose or disturbances

$$R' = \frac{\Delta I}{I} = \frac{I - I_r}{I_r}.$$
(1)

 $R'_{G}$  and  $R'_{D}$  denote the relative changes caused by glucose concentration and the incident light intensity's drift, respectively.  $R'_{G\&D}$  is for both causes. When the variations  $\Delta I$  are not too big, the  $\Delta I$  can be decomposed to the two parts, i.e.,  $\Delta I = \Delta I_{G} + \Delta I_{D}$ .  $\Delta I_{G}$  and  $\Delta I_{D}$  denote the variations of I caused by glucose concentration and the incident light intensity's drift, respectively. Therefore, the equation of  $R'_{G\&D} = R'_{G} + R'_{D}$  would work, too.

#### **2.5** Linearity of Relative Changes in Diffuse Reflection Light Intensity

Using diffuse equation (DE), i.e., the first-order approximate radiative transfer equation (P1-RTE),<sup>22</sup> and Monte-Carlo (MC) simulation,<sup>23</sup> the linearity of R' can be demonstrated using their results. The diffused light intensity can be calculated using Eq. (2), which is solved for a semi-infinite medium by setting an extrapolative boundary



Fig. 2 The schematic of the diffused light in scattering medium.

$$R(\rho) = \frac{1}{4\pi} \left[ z_0 \left( \mu_{\text{eff}} + \frac{1}{r_1} \right) \frac{e^{-\mu_{\text{eff}} \cdot r_1}}{r_1^2} + (z_0 + 2z_b) \left( \mu_{\text{eff}} + \frac{1}{r_2} \right) \frac{e^{-\mu_{\text{eff}} \cdot r_2}}{r_2^2} \right],$$
(2)

where  $\rho$  is the SD separation,  $\mu_{\rm eff}$  is the effective attenuation coefficient, defined as  $\mu_{\rm eff} = \sqrt{3\mu_{\rm a}(\mu_{\rm a} + \mu_{\rm s}')}$ .  $\mu_{\rm a}$  is the absorption coefficient of the medium;  $\mu_{\rm s}'$  is the reduced scattering coefficient defined as  $\mu_{\rm s}' = (1 - g) \cdot \mu_{\rm s}$ , where g is the anisotropy factor, and  $\mu_{\rm s}$  is the scattering coefficient; D is the diffusion coefficient as  $D = [3(\mu_{\rm a} + \mu_{\rm s}')]^{-1}$ .  $z_0 = 1/(\mu_{\rm a} + \mu_{\rm s}')$ ,  $z_{\rm b} = 2D$ ,  $r_1 = [z_0^2 + \rho^2]^{1/2}$ , and  $r_2 = [(z_0 + 2z_{\rm b})^2 + \rho^2]^{1/2}$ . In the glucose measurement,  $R'_{\rm G}$  can be calculated after the

In the glucose measurement,  $R'_{G}$  can be calculated after the diffuse light intensity values with different glucose concentrations are estimated by using Eq. (2) or an MC stimulation program.

The 10% Intralipid solution's parameters<sup>24</sup>  $\mu_a$ ,  $\mu_s$ , g, and n used in the equation and MC simulation are shown in Table 1. The variations of the parameters caused by glucose can be determined according to the equations in Kohl's papers.<sup>25,26</sup> The variation of the absorption coefficient induced by the glucose concentration can be expressed as<sup>25</sup>  $\Delta \mu_a = (\varepsilon_g - f_w^g \cdot \varepsilon_w) \Delta c_g$ , where  $\varepsilon_g$  and  $\varepsilon_w$  are the molar extinction coefficients of glucose and water, respectively, and  $f_w^g$  is the displacement factor between glucose and water. The variations of the refractive index n and anisotropic factor g induced by the glucose concentration

Table 1The parameters of 10% Intralipid used in P1-RTE and MC at1100 to 1400 nm.

Wavelength				
(nm)	$\mu_{a}  ({\rm cm^{-1}})$	$\mu_{s} \text{ (cm}^{-1}\text{)}$	g	п
1100	0.806015	73.5628	0.313	1.459764
1120	0.806015	71.21505	0.313	1.45948
1140	0.806015	69.92356	0.308	1.459209
1160	0.806015	67.782	0.302	1.458951
1180	1.613655	64.60844	0.301	1.458704
1200	2.41967	63.25112	0.303	1.458468
1220	3.22731	61.37735	0.308	1.458242
1240	3.22731	60.25214	0.304	1.458026
1260	3.22731	57.32702	0.306	1.45782
1280	3.22731	55.93885	0.308	1.457622
1300	3.22731	55.56339	0.313	1.457432
1320	4.031699	54.55409	0.32	1.45725
1340	4.839339	53.44438	0.326	1.457076
1360	6.451369	52.00334	0.328	1.456908
1380	6.451369	51.84902	0.326	1.456748
1400	10.48469	51.39153	0.32	1.456593

are expressed as<sup>25</sup>  $\Delta n = 2.5 \times 10^{-5} \Delta c_g$ ,  $\Delta g = 8.45 \times 10^{-6} \Delta c_g$ . For Intralipid solutions, the variation of the scattering coefficient  $\mu_s$  induced by the glucose concentration is<sup>26</sup>  $\Delta \mu_s = -2m\mu_s \Delta c_g$ , where  $m = (1.569 \times 10 - 5\lambda + 0.001)/100$ , and  $\lambda$  is the wavelength (nm).

Figures 3 and 4 show the results of  $R'_{G}$  for the 1100-nm diffuse light from the SD separations of 0 to 3.5 mm.

The  $R'_{G}$  in Figs. 3 and 4 can show an approximate linearity to SD separation. Glucose would induce a simultaneous change in  $\mu_{a}$  and  $\mu'_{s}$  of the tested medium, and the two factors would induce an approximately linear change in R' to SD separation. The linearity caused by glucose could be a comprehensive result.

It also can be found that the diffuse light intensity around the FRP would be relative stable and insensitive to the change of glucose concentration. The values of FRP appear different in Figs. 3 and 4 because of the differences of the two theoretical practices using DE and MC simulations.



**Fig. 3** The result of  $R'_{G}$  calculated using P1-RTE for the medium of 10% Intralipid solution at 1100 nm when glucose concentration varies between in 200 and 2000 mg/dL and the solution without glucose is the reference. The FRP locates at 1.6 mm.



Source-detector separation (mm)

**Fig. 4** The result of  $R'_{G}$  calculated using MC simulation for the medium of 10% Intralipid solution at 1100 nm when glucose concentration varies between in 200 and 2000 mg/dL and the solution without glucose is the reference. The FRP locates at 0.9 mm.

#### 3 Experimental Results and Calculations

#### **3.1** Result of R'<sub>G</sub> in One Short-Term Test

The FRP is found out by the phantom experiment. The relative variations  $R'_{\rm G}$  were calculated for the samples with the glucose concentration of 200 to 2000 mg/dL using Eq. (1) when the  $I_{\rm r}$  is from the sample without glucose. Figure 5 shows some typical results of  $R'_{\rm G}$ .

Figure 6 shows the FRPs of 1100 to 1400 nm by MC when  $\mu_s$  changes  $\pm 5\%$ . The location of FRP is relatively stable when the scattering properties of the medium change a little. The FRPs of MC are different with the experiments because MC is based on the assumption of a semi-infinite medium, while it is actually closer to an infinite medium in the experiments.

#### **3.2** Result of $R'_D$ with Instrument Drift During 48 h

Using the diffuse reflection light intensity results from the first test as the  $I_r$  value, the  $R'_D$  results can be acquired for all samples to demonstrate their drifts in the second to fifth tests. For every sample, the  $R'_D$  primarily shows the influence from the instrument drift.



Fig. 5 The results of  $R'_{\rm G}$  for the first test in the medium of 10% Intralipid solution when glucose concentration varies between in 400 and 2000 mg/dL with the interval of 400 mg/dL and the solution without glucose is the reference at 1100 nm. The FRP locates at ~1.9 mm.



**Fig.6** FRP of 1100 to 1400 nm by MC when  $\mu_s$  changes  $\pm 5\%$ .

Some typical  $R'_D$  results are shown in Fig. 7 and the  $R'_D$  from different SD separations appear approximately similar. It can, therefore, be assumed that there is an equivalent  $R'_D$  for an arbitrary pair of SD separations of 0.47 to 3.095 mm as shown in

$$R'_{\mathrm{D},\rho_1} = \frac{\Delta I_{\rho_1}}{I_{\rho_1}} = \frac{\Delta I_{\rho_2}}{I_{\rho_2}} = R'_{\mathrm{D},\rho_2},\tag{3}$$

where  $\rho_1$  and  $\rho_2$  are two different SD separations.

Based on Eq. (3), the light source intensity drift can be reduced by differential calculation between the  $R'_{\rho}$  of two SD separations. As shown in

$$dR'_{G,\rho_1-\rho_2} = R'_{G\&D,\rho_1} - R'_{G\&D,\rho_2}.$$
(4)

The glucose-related information in  $dR'_{G}$  after differential calculation is a combination of the glucose information from  $\rho_1$  and  $\rho_2$ . If one of the SD separations  $\rho_2$  is the FRP,  $R'_{G\&D,\rho_2}$  does not contain any glucose information, i.e.,  $R'_{G\&D,\rho_2} \approx R'_{G,\rho_2}$ . It can be derived that  $dR'_{G,\rho_1-\rho_2}$  would be the corrected  $R'_{G}$  at  $\rho_1$ , i.e.,  $dR'_{G,\rho_1-\rho_2} \approx R'_{G,\rho_1}$ . So, the correction can be described as

$$R'_{G,\rho} = R'_{G\&D,\rho} - R'_{D,\rho_{FRP}}.$$
(5)

 $\rho$  is any SD separation where the spectral data need to be corrected.

Equation (5) can also be described as

$$\Delta I_{\rho} = \frac{I_{\rho}}{I_{\rho_{\rm FRP}}} \Delta I_{\rho_{\rm FRP}}.$$
(6)

Therefore, using Eq. (6), the change of light intensity at any position  $(\Delta I_{\rho})$  can be estimated by the drift at the FRP  $(\Delta I_{\text{FRP}})$  when it takes the FRP as the reference position.

It should be noted that the characteristics of the synchronic drift might not occur with weaker diffuse light signals, which are reflected at the distances far from the light source. For the wavelengths where the medium has stronger absorption, the available SD separations would be very small.

#### 3.3 Correcting based on the FRP

From Eq. (3), the FRP can directly indicate the drift  $R'_{\rm D}$  even for all available positions. When the measurement is only disturbed by the drift of incident light intensity or glucose concentration variation, the drifted  $R'_{\rm G}$  can be corrected for all SD separations when the  $R'_{\rm G\&D}$  deducts the drift  $R'_{\rm D}$  at  $\rho_{\rm FRP}$ , as shown in Eq. (5).

Figure 8(a) shows the  $R'_{G\&D}$  results, including  $R'_{G}$  and  $R'_{D}$ , for 1000 mg/dL glucose solution samples referencing to the solution without glucose. The corrected  $R'_{G}$  result is shown in Fig. 8(b).

Using the correction method based on FRP, the R' results from all samples and all tests are corrected. Figure 9 shows the correction results for some typical samples in the last test, which started 48 h after the first test. And all the samples' R' are calculated using Eq. (1), in that the  $I_r$  is the reference light intensity measured in the solution without glucose.

According to Eq. (4), the light source drift can be reduced by differential calculation,  $dR'_{G,\rho_1-\rho_2} = R'_{G\&D,\rho_1} - R'_{G\&D,\rho_2}$ . But the result related to the two positions  $dR'_{G,\rho_1-\rho_2}$ , will be different from any result of a single position. Figure 10 shows two results after correction. As can be seen, they are different from the short-term test shown in Fig. 5.



**Fig. 7** The result of  $R'_D$  calculated at 1100, 1180, 1260, and 1340 nm for the second to fifth test in the medium of 10% Intralipid solution as the first test is for reference: (a) 1100 nm, (b) 1180 nm, (c) 1260 nm, and (d) 1340 nm.



**Fig. 8** R' results of the all tests at 1100 nm for the 10% Intralipid solution with 1000 mg/dL glucose concentration: (a)  $R'_{G&D}$  before correction and (b)  $R'_{G}$  after correction.

In Fig. 10, the horizontal axis shows that  $\rho_1$ , and  $\rho_2$  are the reference positions. In Fig. 10(a),  $\rho_2$  is the near light source,  $\rho_2 = 1.0$  mm, and FRP is at 1.9 mm. In Fig. 10(b),  $\rho_2$  is far from the light source,  $\rho_2 = 2.5$  mm. As can be seen, choosing  $\rho_2$  far from the light source does not contribute to a better result due to the increase of noise after differential calculation, although the glucose information increases at the same time. The selection of  $\rho_1$  and  $\rho_2$  could deeply influence the result of absolute change of light intensity  $dI'_{G,\rho_1-\rho_2}$ . The detection limit can be evaluated by the comparison of  $dI'_{G,\rho_1-\rho_2}$  and the level of noise.

### **3.4** Correction Results of all Spectra at 1100 to 1400 nm

The diffuse reflection spectra in the wavelength ranging from 1100 to 1400 nm are corrected using the reference position of FRP. Similarly, the absolute light intensity can be corrected using the corrected R' and its initial value. Figure 11 shows the absolute light intensity results for 1000 mg/dL from 1100 to 1400 nm before and after correction for the SD separation of 0.595 mm. The coefficients of variation (CVs) of the spectra from the original and corrected results are compared in

Han et al.: Floating reference position-based correction method for near-infrared...



**Fig. 9** The R' results of the fifth test at 1100 nm for the 10% Intralipid solution with glucose concentration of 400 to 2000 mg/dL with the interval of 400 mg/dL: (a)  $R'_{G\&D}$  before correction and (b)  $R'_{G}$  after correction.



Source–detector separation of  $\rho_1$  (mm)

Source–detector separation of  $\rho_1(mm)$ 

**Fig. 10** The  $dR'_{G,\rho_1-\rho_2}$  results of the fifth test at 1100 nm for the 10% Intralipid solution with glucose concentration of 400 to 2000 mg/dL with the interval of 400 mg/dL: (a)  $dR'_{G,\rho_1-\rho_2}$  of  $\rho_2 = 1.0$  mm and (b)  $dR'_{G,\rho_1-\rho_2}$  of  $\rho_2 = 2.5$  mm.



Fig. 11 Diffuse reflection spectra of the 10% Intralipid solution with 1000 mg/dL glucose concentration before and after correction at SD separation of 0.595 mm: (a) before correction and (b) after correction.



Fig. 12 Comparison of CVs of diffuse reflection spectra of the 10% Intralipid solution with 1000 mg/dL glucose concentration before and after correction at SD separation of 0.595 mm.

Fig. 12. It is clear that the CVs improved from 0.01 to 0.025 before correction to less than 0.004 after correction.

#### 3.5 Modeling and Predicting Glucose Concentrations Using Corrected Spectra

Partial least square and leave-one-out cross validation are used for modeling and predicting the glucose concentrations in 10% Intralipid. It is necessary to use the spectra from those positions, which are far away from the reference FRP, because their signals should be sensitive to glucose. For the wavelengths of 1100 to 1400 nm, the FRPs distribute between 1.2 and 2.0 mm. Therefore, the SD separations of 1.2 to 2.0 mm are not available. The data from greater than 3.2 mm could not be used due to the weak signals at some wavelengths. By randomly choosing spectra from the five tests for every sample, we can obtain a set of data to test the prediction with the disturbance of instrument drift. Using these data, the prediction has an unsatisfactory root mean square error of cross validation (RMSECV) result in the cross validation, as shown in the first RMSECV column result of Table 2. When all of the spectra are corrected using our approach, the RMSECV values are closer to the best values obtained from the spectra recorded in one test, which takes  $\sim 10$  min and can be called "short-term monitoring." The 
 Table 3
 RMSECV results of the prediction using other positions as reference.

SD separation (mm)			After differential measurement		
$\rho_1$	ρ2		RMSECV (mg/dL)	R	
0.595	Less than FRP	0.72	355.6	0.687	
		0.97	264.2	0.829	
	Near to FRP	1.845	69.1	0.992	
		1.97	80.8	0.986	
	Greater than FRP	2.845	120.9	0.947	
		2.97	212.2	0.890	

average RMSECV values of the five short-term tests are listed in the third RMSECV column of Table 2. Moreover, the SD separations, which are near the FRP, should not be used for the glucose measurement, since there the signals got a worse prediction result due to being insensitive to the glucose concentration's variation.

Table 3 shows the RMSECVs of prediction after differential measurement between two SD separations. Choose  $\rho_1 = 0.595$  as the detection position, and the referenced positions are the SD separations that are less than FRP, near FRP, and greater than FRP, respectively. For the wavelengths of 1100 to 1400 nm, FRP is between 1.2 and 2.0 mm (based on short-term experiment). The result shows that if  $\rho_2$  is less than FRP, the differential result could decrease the glucose-related information because the two positions are too close to each other, and the prediction error is bigger than the result only using one position of  $\rho_1$ . If  $\rho_2$  is near to FRP, glucose information would be lost less and the RMSECVs using two positions are similar to the result using only one position of  $\rho_1$ . For the  $\rho_2$  far away from the FRP, the noise from  $\rho_2$  greatly increases and the RMSECVs decrease after differential of the two positions.

In Tables 2 and 3, the prediction of glucose after using the reference position of the accurate FRPs or of the positions that are near to FRP show good results, which is closer to the result

SD separation (mm)		Before correction		After FRP correction		In short-term test	
		RMSECV (mg/dL)	R	RMSECV (mg/dL)	R	RMSECV (mg/dL)	R
Less than FRP	0.595	342.5	0.712	76.7	0.990	51.5	0.995
	0.72	369.1	0.666	87.5	0.985	64.8	0.993
	0.97	218.6	0.883	97.2	0.961	57.7	0.994
Near to FRP	1.845	894.1	-0.962	414.0	0.579	332.1	0.684
	1.97	206.8	0.895	394.9	0.617	296.6	0.792
Greater than FRP	2.845	250.3	0.846	214.9	0.891	131.8	0.932
	2.97	265.6	0.827	277.2	0.811	152.6	0.916

Table 2 RMSECV results of the prediction using the reference position of FRP.

from the short-term test. This is because the spectral data collected near the FRP carry little glucose-related information, so the corrected R' may reserve most original glucose information at  $\rho_1$ . The prediction accuracy of selecting accurate FRPs or the positions near FRP as reference are similar. In real use, we suggest the FRPs of the subject should be measured first and then select the position that is easy to measure near the FRP. But the correction results using an accurate FRP have advantages of building a model because the corrected spectra and original spectra can be used for mutual prediction.

#### 4 Conclusions

In this paper, we present an FRP-based correction method for NIR diffuse reflection spectra, which we verified as an effective approach to reduce the drift caused by the variation of incident light intensity. This correction will be helpful for improving the stability of spectra during long-term BGC monitoring. The correction can be easily performed for all spectra at required positions when their relative changes of diffuse light intensity can be estimated by an FRP because changes in these relative variations are approximately linear with SD separations.

Moreover, the correction can also be used to reduce the drifts from other sources of disturbance because their relative drifts in incident light intensity may yield similar characteristics of linearity. As shown in Figs. 2, 3, and 5, it is clear that glucose could also induce a linear change with a range of positions. Indeed, this characteristic of linearity is possessed by many components in solution or in blood when the available positions are limited to a reasonable range. We are also planning to reduce some mixed disturbances that linearly affect the relative change of diffuse light intensity by decomposing these mixed lines. In this paper, we made a preliminary successful attempt even though only the line of the drift from incident light is deduced for every signal.

The correction method presented in this paper is significant for 48-h glucose concentration monitoring. The analysis method in this paper can also be referenced to eliminate other disturbances in a linear fashion and obtain high-quality spectral signals.

#### Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

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