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(21) International Application Number: PCT/US93/06890 (22) International Filing Date: 22 July 1993 (22.07.93) (30) Priority data: 07/917,998 24 July 1992 (24.07.92) US (71) Applicant: FUTREX, INC. [US/US]; P.O. Box 2398, Gaithersburg, MD 20886 (US). (72) Inventor: ROSENTHAL, Robert, D. ; 9805 Hallowell Place, Gaithersburg, MD 20879 (US). (74) Agents: ROTHWELL, G., Franklin et al.; Rothwell, Figg, Ernst & Kurz, 555 Thirteenth Street, N.W., # 701 East, Washington, DC 20004 (US).		(81) Designated States: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: METHOD AND MEANS FOR GENERATING SYNTHETIC SPECTRA ALLOWING QUANTITATIVE MEASUREMENT IN NEAR INFRARED MEASURING INSTRUMENTS 		
(57) Abstract A method and means for generating synthetic spectra allowing quantitative measurement utilizes dual chip (12, 14) alternatively energized IREDs (10) with optical bandpass filter(s) (22, 24) passing two optical bands which has been combined with curvilinear interpolation to be utilized in a low cost small size quantitative measuring instrument.		

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METHOD AND MEANS FOR GENERATING SYNTHETIC SPECTRA
ALLOWING QUANTITATIVE MEASUREMENT IN NEAR INFRARED
MEASURING INSTRUMENTS

BACKGROUND OF THE INVENTION

5 Cross-Reference to Related Applications

 This application is a continuation-in-part of U.S. Patent Application Serial No. 07/588,628 filed September 26, 1990 and which will issue as U.S. Patent No. 5,134,302, on July 28, 1992.

10 Field of the Invention

 This invention relates to improvements in near-infrared quantitative measuring instruments and particularly, to a method and means for generating synthetic spectra for such instruments.

15 Background and Prior Art

 Near-infrared quantitative measuring instruments have been available for approximately 20 years. These instruments have proven to be highly accurate and simple to use for the measurement of chemical
20 constituents in many different types of materials. For example, near-infrared instruments are commonly used in the grain industry for determining the protein of wheat and barley, in the food industry for measuring various organic constituents within food, in the chemical

process industry to determine the chemical constituents within a production product, and in the medical field for non-invasively determining such items as body fat percentage.

5 There are three general types of near-infrared measuring instruments. Reflectance-type instruments normally measure between 1,100 and 2,500 nanometers to provide accurate measurement of materials that have a consistent surface and require access to only one side
10 of the product being measured. Transmission-type measurements are available that operate between 600 and 1,100 nanometers and are able to measure almost any type of product without sample preparation provided that access is available to both sides of the measured
15 product. The third type of near-infrared instrument is the interactance type which normally operates between 600 and 1,100 nanometers. In this type of instrument, light energy is directed into a body of a product and on the same side of the body at some distance away, the
20 internal reflected light is measured.

 In any of the above-described type of near-infrared measuring instruments, the use of discrete filters or the use of full scanning instruments are known. An example of the use of a filter-type approach
25 is shown in U.S. Patent No. 4,286,327.

 In many applications, either discrete filter or full scanning instruments will provide similar accuracy. However, there are some applications where the typical discrete filter-type instruments do not
30 provide sufficient information. Examples of this are applications where advanced mathematical treatments such as Partial Least Square or Principle Component Analysis are applied. In such approaches, a large

number of wavelengths are needed to provide the necessary calibration coefficients.

One major disadvantage of the full scanning instruments is that they are considerably more
5 expensive than the discrete filter instruments. Thus, the desire has been to develop techniques that allow discrete filter instruments to provide the same sensitivity and versatility as full scanning instruments. One such approach is described in U.S.
10 Patent No. 4,627,008 where the use of curvilinear interpolation allows development of synthetic spectra from a discrete filter instrument.

However, in the measurement of very subtle constituents, e.g., non-invasive measurement of the
15 level of glucose in the blood stream with a low cost portable instrument, accurate knowledge of spectra is required at many wavelengths. There is a need in the art to generate such spectra to provide a meaningful quantitative measuring instrument.

20 U.S. Patent No. 4,286,327 teaches that a group of IREDs, each with a separate narrow bandpass filter in front of it, can be consecutively illuminated, thereby generating meaningful optical information. In such patent, a separate narrow bandpass filter is required
25 for each wavelength to be measured. However, for a low cost portable instrument where broad spectrum information is required, it becomes essentially impractical to provide the number of narrow bandpass filters that are required. A size limitation, combined
30 with the need for low cost, precludes such approach.

For example, research has shown that on some individuals, accurate measurement of blood glucose can be obtained by using a combination of wavelengths between 640 nanometers and 1,000 nanometers. These

studies have also shown that different combinations of wavelengths are required for different individuals because of the body composition differences between people. For example, if cholesterol or glucose is
5 desired to be measured, those constituents are in such minute quantities compared to the presence of water, fat and protein in the body that they are difficult to measure without multiple wavelengths. Thus, the need
10 in the art exists to provide a low cost, portable, simple instrument and yet have the instrument provide the equivalent of wavelengths at every 1 nanometer between 640 to 1,000 nanometers so as to be useful over a broad population.

SUMMARY OF THE INVENTION

15 This invention provides a method and means for producing synthetic spectra for use in quantitative near-infrared measuring instruments which can be utilized in curvilinear interpolation instruments and which provide two wavelengths from a single IRED by
20 using a dual chip IRED, and provide multiple outputs by utilizing dual bandpass filters with a single IRED. Thus, two wavelengths at a very narrow tolerance can be produced from a single IRED.

BRIEF DESCRIPTION OF THE INVENTION

25 Fig. 1(A) shows a spectra of blood glucose values for a first individual.

Figs. 1 (B) and 1(C) show an expanded view of the Fig. 1(A) spectra.

30 Fig. 2(A) shows a spectra of blood glucose values for a second individual.

Figs. 2(B) and 2(C) show an expanded view of the Fig. 2(A) spectra.

Fig. 3(A) shows a spectra of blood glucose values for a third individual.

Figs. 3(B) and 3(C) show an expanded view of the Fig. 3(A) spectra.

5 Fig. 4(A) shows a spectra of blood glucose values for a fourth individual.

Figs. 4(B) and 4(C) show an expanded view of the Fig. 4(A) spectra.

10 Figs. 5(A) and 5(B) are schematics of a dual chip IRED showing different arrangements of such IREDs with optical bandpass filters.

Figs. 6(A) and 6(B) are typical spectra for both light emitting diodes (LEDs) and infrared emitting diodes (IREDs).

15 Fig. 7(A) is spectra of a typical narrow bandpass filter and 7(B) illustrates a special narrow bandpass filter for two different bands.

20 Figs. 8(A) and 8(B) are schematics of an IRED having three chips and illustrating different arrangements of such IREDs with optical bandpass filters.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

To study how many wavelengths are required for accurate quantitative measurement using IRED
25 techniques, an interactive study of accuracy of generating a synthetic spectra using the curvilinear approach taught by U.S. Patent No. 4,637,008 versus actual spectra in different people was performed. For example, in wavelengths between 640 to 1,000
30 nanometers, it was found that 12 discrete wavelengths properly located in the spectra can generate a synthetic spectra that is equal in accuracy to when one "real spectra" is compared to another "real spectra."

("Real spectra" is defined as a spectra obtained from a high quality scanning spectrophotometer.)

For typical people, it was discovered that the following 12 wavelengths would provide the basis for generating synthetic spectra. (These wavelengths allow some reasonable tolerance, approximately ± 2 nanometers each.) These wavelengths are set forth in the following table.

TABLE I

	<u>GROUP A</u>		<u>GROUP B</u>	
	<u>Filter Number</u>	<u>Wavelength</u>	<u>Filter Number</u>	<u>Wavelength</u>
	1	640 nm	7	878 nm
	2	688	8	916
15	3	698	9	946
	4	754	10	964
	5	804	11	974
	6	840	12	1000

Figs. 1(A)-(C) through 4(A)-(C) contain spectra from four different individuals, respectively, covering a broad range of race, body composition and gender. Each of the figures provide an overlay of "real data," i.e., data which was actually measured by a scanning spectrophotometer at every one nanometer interval, represented in an expanded scale, with a synthetic spectra generated using a curvilinear technique utilizing the 12 wavelengths set forth above. On each of these curves in Figs. 1(A)-(C) through 4(A)-(C), the correlation squared term (R^2) is given as well as the standard error between the "real data" versus the synthetic spectra. As can be seen, the synthetic spectra is very accurate as compared to the real spectra.

Also presented in Figs. 1(A)-(C) through 4(A)-(C) are the R squared and the standard error of one real spectra overlaid with another real spectra of the same individual, represented as "Real vs. Real", at approximately the same period in time (measured within a few minutes of each other). (Note the figures do not show the curves of the real spectra overlaying.) As illustrated in Figs. 1(A)-(C) through 4(A)-(C), the synthetic spectra and the real spectra accuracy numbers are quite close to the accuracy number between two real spectra. Moreover, when regression analysis against known blood glucose values was performed with the synthetic spectra analysis of the present invention, it provided essentially identical accuracy as such analysis using real spectra.

A low cost method of implementing this invention is shown in Figs. 5(A) and 5(B). In each of these figures, there is shown a light emitting diode 10 using two light emitting chips 12 and 14 in the single diode. The chips may be alternately energized through leads 16 as is known in the art. For example, a single diode may be obtained on the market that provides both red and green light, depending on the way it is powered. In Figs. 5(A) and 5(B), the single diode 10 comprises the two chips 12 and 14. Chip 14 would provide energy in the region of wavelengths Group A and chip 12 would provide energy in the region of wavelengths Group B from Table I above.

This can be further understood with reference to Figs. 6(A) and 6(B) which are taken from "Opto Electronic Components Data Book 1988" of Stanley Electric Co., Ltd. In these figures, typical spectra for both LEDs and IREDs are shown. For example, wavelength # 6 and wavelength # 12 from Table I above

can be generated using two chips 12 and 14 in a single IRED 10, namely chips AN and DN. Thus, the wavelength region for wavelength # 6 in Table I would be from the chip DN, i.e., chip 14, and wavelength # 12 would be a chip of the characteristics AN, i.e., chip 12.

Set forth below in Table II are the same wavelengths as in Table I above, but with the corresponding chips selected from Figs. 6(A) and 6(B). Stated differently, depending on how the IRED is powered, i.e., whether chip 12 or chip 14 is energized, either energy for wavelength 12 or wavelength 6 is illuminated.

TABLE II

<u>GROUP A</u>		<u>GROUP B</u>	
Filter Number	Wavelength	Filter Number	Wavelength
1	640 nm AR or BR	7	878 CN or DN
2	688 BR or PR	8	916 CN or BN
3	698 PR	9	946 AN or BN
4	754 PR	10	964 AN or CN
5	804 PR or DN	11	974 AN
6	840 DN Type	12	1000 AN Type

Also as shown in Fig. 5(A), there is a bandpass filter 20 with two bandpasses. While in Fig. 2(B), there are separate optical bandpass filters 22 and 24, filter 22, for example, with a bandpass for # 6 wavelength in the table above, and optical filter 24 with a bandpass for # 12 wavelength in the table above. The bandpass filter 20 of Fig. 5(A) could pass two bands, for example, as shown in Fig. 7(B). In other words, Fig. 7(A) illustrates a spectra of a typical narrow bandpass filter which would be filter 24 in Fig. 5(B). Fig. 7(B) illustrates the transmission from a special narrow dual bandpass filter that allows light

to pass at two different bands, e.g., 840 and 1,000 nanometers.

When the dual chip IRED in Fig. 5(A) is utilized in a single filter with two bandpasses as shown in Fig. 7(B), and when the first chip of the IRED is illuminated, wavelength # 6 is available. When that chip is de-energized and the second chip is powered, then wavelength # 12 of the above table is illuminated.

Utilizing this invention, only 6 IREDs and 6 filters are required to generate the identical data that would normally take 12 optical filters in combination with 12 individual IREDs. Thus, the number of parts is reduced by a factor of 2 which means a significant increase in reliability as well as the cost being reduced by a factor of 2. Moreover, this invention reduces the space requirements and such is essential for a portable pocket-size instrument.

In accordance with another embodiment of the present invention, a low cost apparatus for implementing the present invention is shown in Figs. 8(A) and 8(B). In each of these figures, there is shown a light emitting diode 30 using three light emitting chips 33, 34 and 35 in the single diode. The chips may be alternately energized through leads 31 as is known in the art, emitting the wavelengths, for example, as shown above in Table I.

Also as shown in Fig. 8(A), there is a bandpass filter 32 with three bandpasses which can pass three bands, or wavelengths of interest, substantially similar to spectra illustrated in Fig. 7(B). In Fig. 8(B), three separate optical bandpass filters 36, 37 and 38 are utilized to pass wavelengths of interest similar to the spectra illustrated in Fig. 7(A).

Utilizing this invention, only 4 IREDs and 4 filters are required to generate the identical data that would normally take 12 optical filters in combination with 12 individual IREDs. Thus, the number
5 of parts is significantly reduced which means a significant increase in reliability as well as the cost reductions.

In another embodiment of present invention, a synthetic spectra can be generated equal in accuracy to
10 a "real spectra" using wavelengths between approximately 600 to approximately 1,100 nanometers, from discrete wavelengths located within the spectra. In addition to the wavelengths disclosed above, utilizing wavelengths at approximately 1023 and
15 approximately 1080 nanometers can be used to create an accurate synthetic spectra in accordance with the present invention.

In still another aspect of the present invention, a synthetic spectra can be generated equal in accuracy
20 to a "real spectra" in wavelengths between approximately 600 to approximately 1100 nanometers, from 14 discrete wavelengths properly located within the spectra. The following 14 wavelengths provide a basis for generating a synthetic spectra. (These
25 wavelengths allow some reasonable tolerance, approximately ± 2 nanometers each.) These wavelengths are set forth in the following table.

TABLE III

<u>GROUP A</u>		<u>GROUP B</u>	
<u>Filter</u>	<u>Wavelength</u>	<u>Filter</u>	<u>Wavelength</u>
<u>Number</u>		<u>Number</u>	
5	1 604 nm	8 833 nm	
	2 658	9 860	
	3 702	10 877	
	4 723	11 910	
	5 746	12 932	
10	6 786	13 953	
	7 810	14 990	

A low cost method and apparatus for implementing the present invention is essentially the same as disclosed above in connection with Figures 5(A) and 5(B). In this embodiment, seven dual chip IREDs are utilized to create the desired wavelengths as described above. Also, a single bandpass filter having two bandpasses or two bandpass filters can be utilized as disclosed in Figures 5(A) and 5(B).

Set forth below in Table IV are examples of types of IREDs which can be used to create the desired wavelengths as set forth in Table III above.

TABLE IV

<u>LED #</u>	<u>Manufacturer</u>	<u>Part #</u>	<u>Wavelength</u>
25	1 Stanley	MAA33685	604 nm
	2 Gilway	E-169	658
	3 Quantum	TI-746	702
	4 Quantum	TI-746	723
	5 Quantum	TI-746	746
30	6 Stanley	DN 306	786
	7 Stanley	DN 306	810
	8 Stanley	DN 306	833
	9 Stanley	DN 306	860
	10 Stanley	DN 306	877
35	11 Stanley	CN 306	910
	12 Stanley	AN 306	932
	13 Stanley	AN 306	953
	14 Stanley	AN 306	990

Utilizing this invention, only 7 IREDs and 7 filters are required to generate the identical data that would normally take 12 optical filters in combination with 12 individual IREDs. Thus, the number of parts is significantly reduced which means a significant increase in reliability as well as the cost reductions.

It is the intention not to be limited by this specific embodiment but only by the scope of the appended claims. For example, the present invention is not intended to be limited to the use of twelve or fourteen wavelengths (and, correspondingly, six or seven dual chip IREDs) to create the synthetic spectra.

The present invention is intended to encompass, inter alia, the use of dual or other multiple chip IREDs in an instrument for generating a synthetic allowing quantitative measurements.

I claim:

1. A quantitative near-infrared analysis instrument for non-invasive measurement of a blood analyte present in a body part of a subject, said analysis instrument comprising:

5 (a) an introducing means comprising a near-infrared energy source for introducing near-infrared energy into blood present in a body part of a patient, said near infrared energy source comprising at least one infrared emitting diode having at least two chips
10 and producing at least two separate wavelengths;

(b) detecting means for detecting near-infrared energy emerging from the body part; and

(c) processing means for calculating a synthetic spectra for curvilinear interpolation based upon
15 signals from said detection means.

2. The near-infrared analysis instrument of claim 1, wherein said, at least one, infrared emitting diode having at least two chips is used in combination with a filter means for passing two separate
5 wavelengths.

3. The near-infrared analysis instrument of claim 2, wherein said filter means is a single filter having two bandpasses.

4. The near-infrared analysis instrument of claim 2, wherein said filter means comprises separate filters, each with a single bandpass.

5. The near-infrared analysis instrument of claim 1, wherein said at least one infrared emitting diode having at least two chips comprises six infrared emitting diodes.

6. A quantitative near-infrared analysis instrument for non-invasive measurement of a blood

analyte present in a body part of a subject, said instrument comprising:

5 (a) an introducing means comprising a near-infrared energy source for introducing near-infrared energy into blood present in a body part of a patient, said near infrared energy source comprising six
10 infrared emitting diodes each having at least two chips and wherein each of said two chips produces a separate wavelength;

(b) detecting means for detecting near-infrared energy emerging from the body part and generating a signal based upon said separate wavelength from each of
15 two chips from said six infrared emitting diodes; and

(c) processing means for calculating a synthetic spectra for curvilinear interpolation based upon the signals generated from said detection means.

7. A quantitative near-infrared analysis instrument for non-invasive measurement of a blood analyte present in a body part of a subject, said analysis instrument comprising:

5 (a) an introducing means comprising a near-infrared energy source for introducing near-infrared energy into blood present in a body part of a patient, said near infrared energy source comprising seven
10 infrared emitting diodes each having at least two chips and wherein each of said two chips produces a separate wavelength;

(b) detecting means for detecting near-infrared energy emerging from the body part and generating a signal based upon said separate wavelength from each of
15 two chips from said seven infrared emitting diodes; and

(c) processing means for calculating a synthetic spectra for curvilinear interpolation based upon the signals generated from said detection means.

8. The near-infrared analysis instrument of claim 7, wherein each of said seven infrared emitting diodes having at least two chips is used in combination with a filter means for passing two separate
5 wavelengths.

9. The near-infrared analysis instrument of claim 8, wherein said filter means is a single filter having two bandpasses.

10. The near-infrared analysis instrument of claim 8, wherein said filter means comprises separate filters, each with a single bandpass.

11. The near-infrared analysis instrument of claim 7, wherein said seven infrared emitting diodes emit energy at selected wavelengths from approximately 600 nanometers to approximately 1100 nanometers.

12. A quantitative near-infrared analysis instrument for non-invasive measurement of a blood analyte present in a body part of a subject, said analysis instrument comprising:

- 5 (a) an introducing means comprising a near-infrared energy source for introducing near-infrared energy into blood present in a body part of a patient, said near infrared energy source comprising at least one infrared emitting diode having three chips and
10 producing at least three separate wavelengths;
- (b) detecting means for detecting near-infrared energy emerging from the body part; and
- (c) processing means for calculating a synthetic spectra for curvilinear interpolation based upon
15 signals from said detection means.

1 / 9

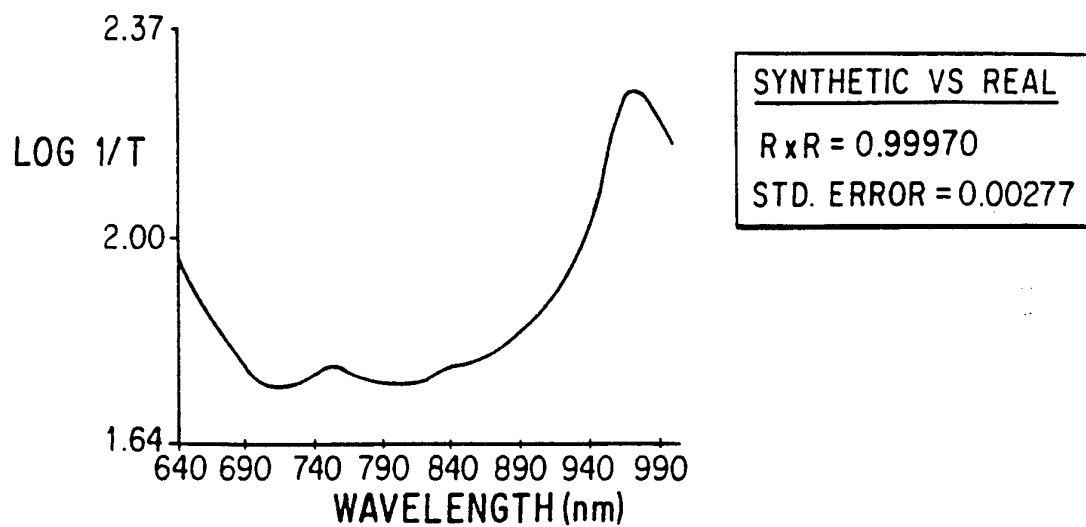


FIG. 1A

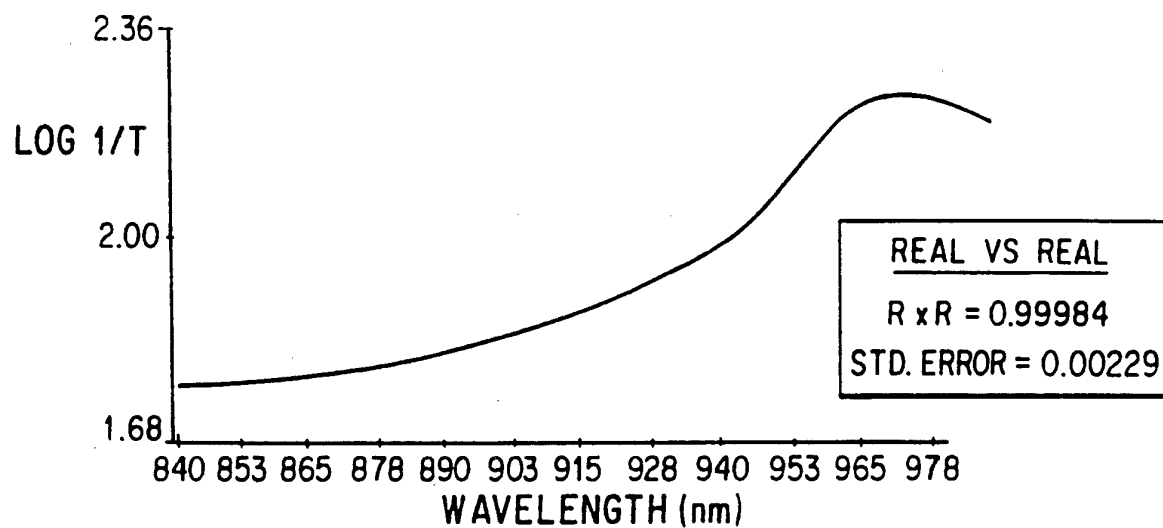


FIG. 1B

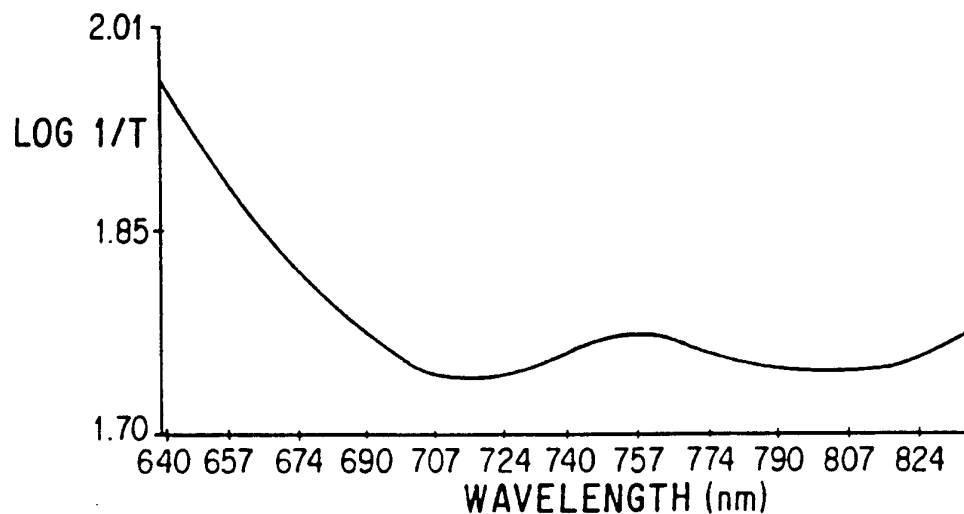


FIG. 1C

2 / 9

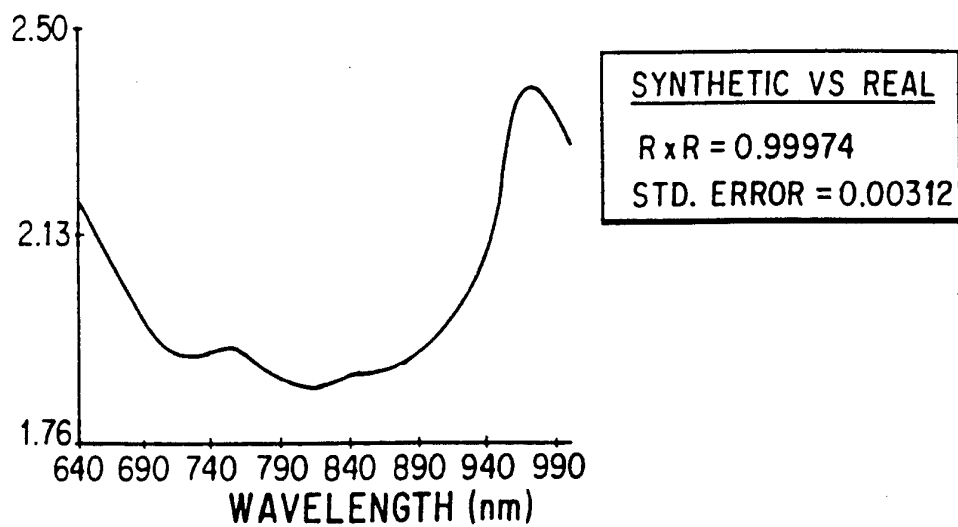


FIG. 2A

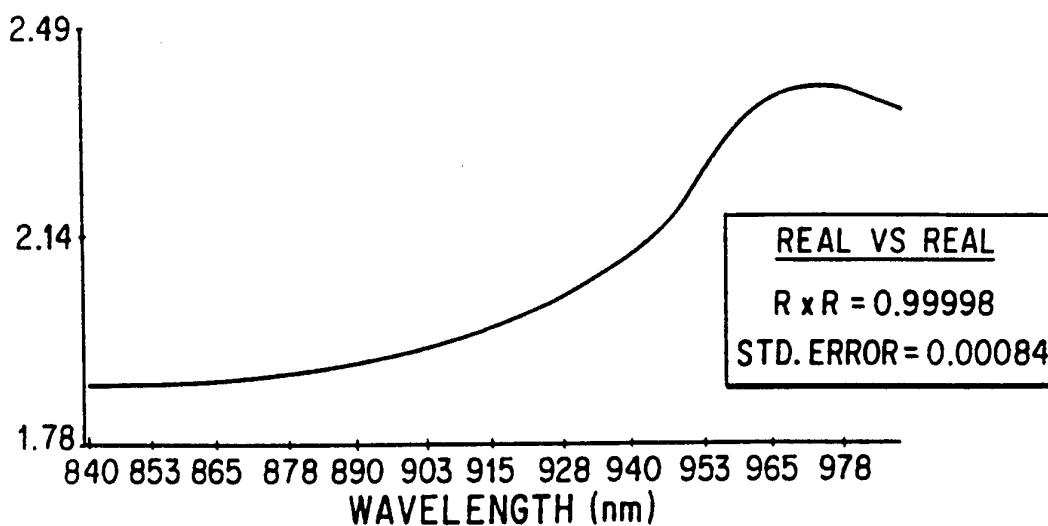


FIG. 2B

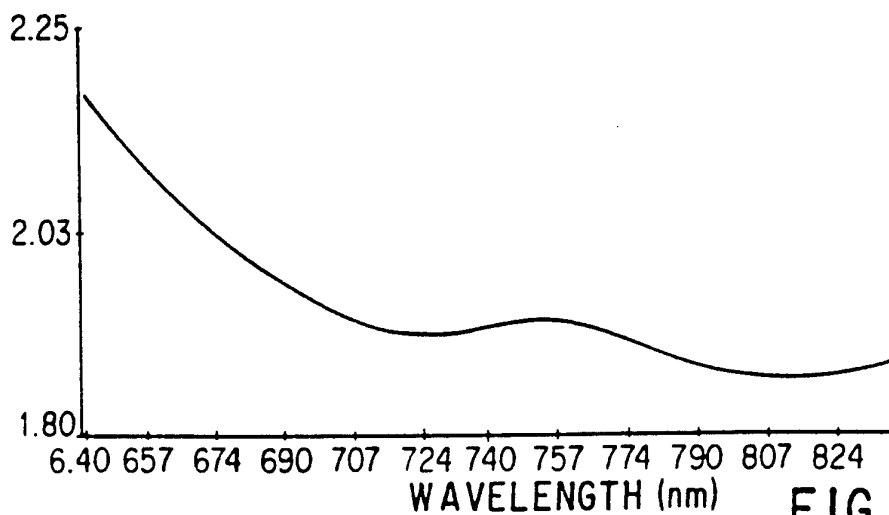


FIG. 2C

3 / 9

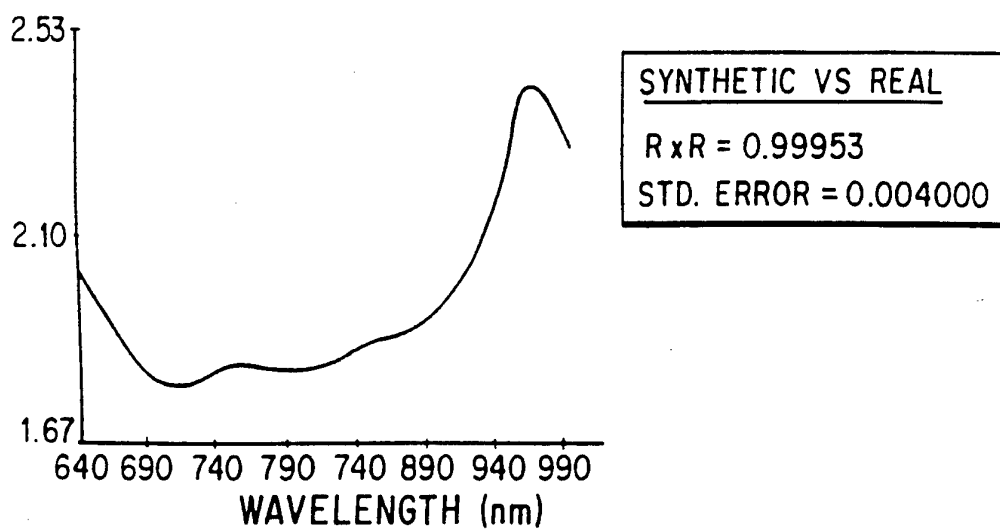


FIG. 3A

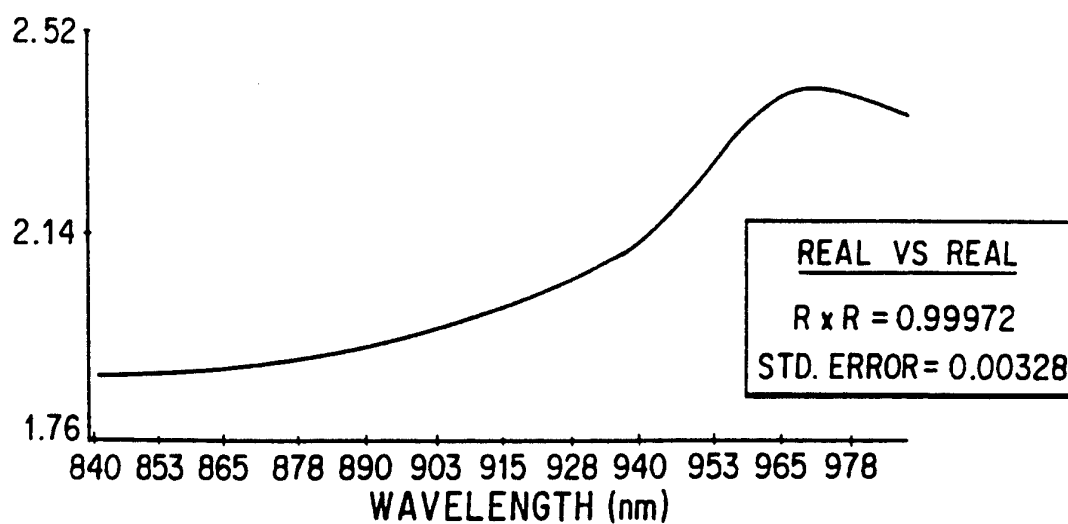


FIG. 3B

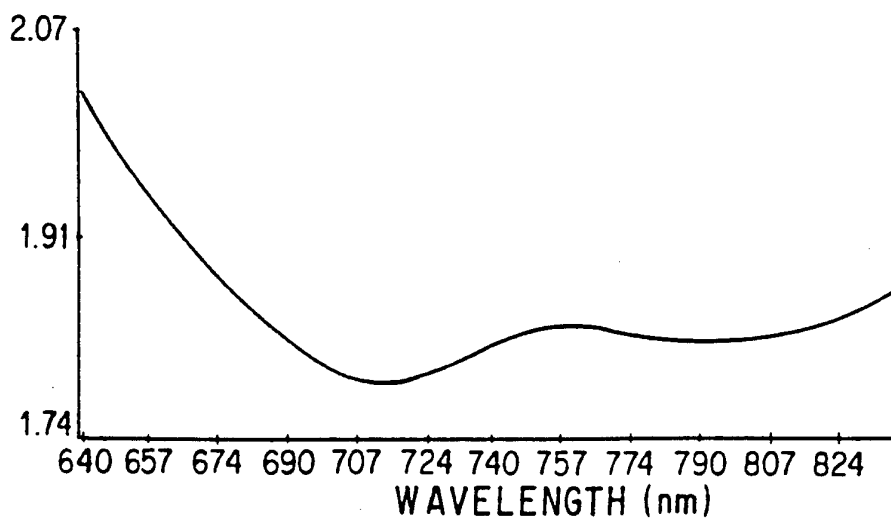
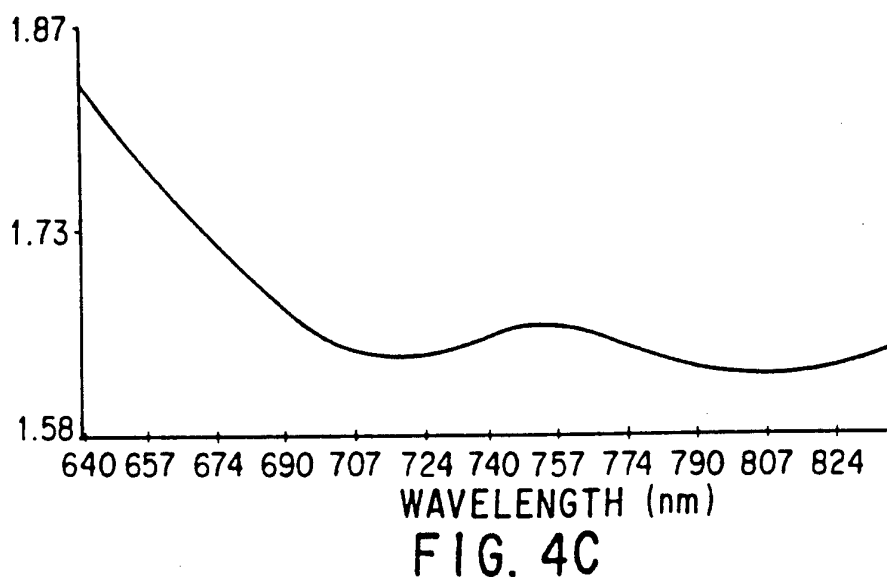
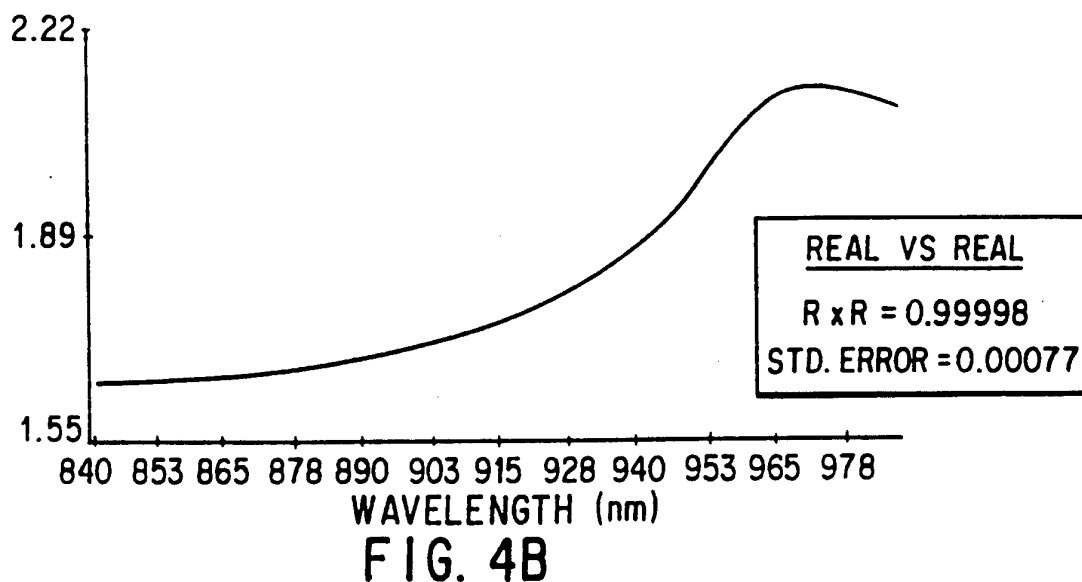
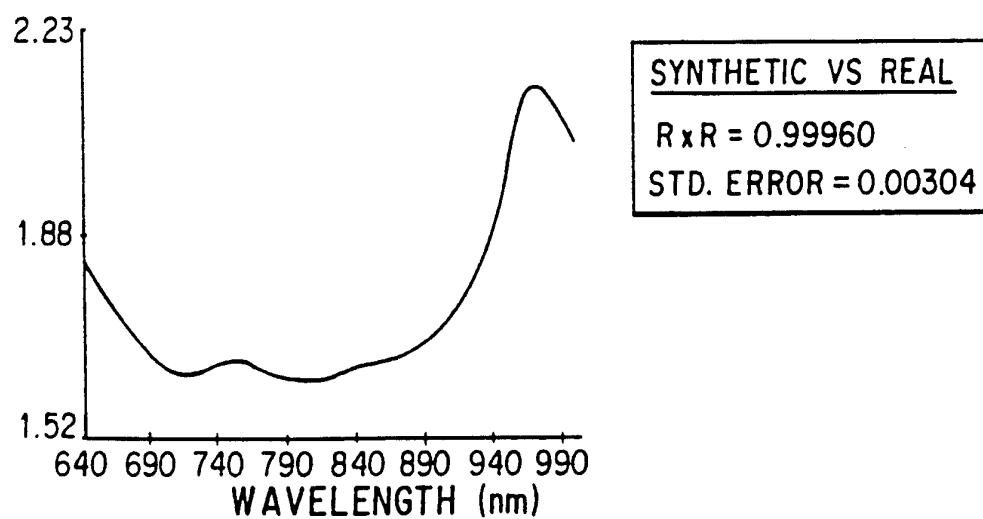


FIG. 3C

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5 / 9

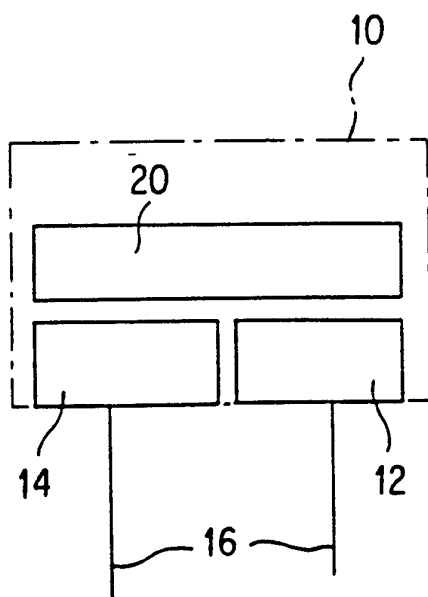


FIG. 5A

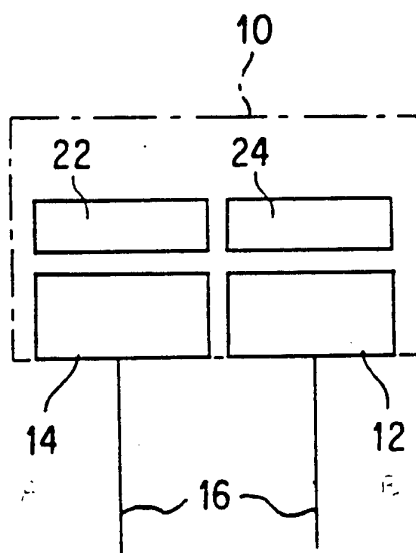


FIG. 5B

6/9

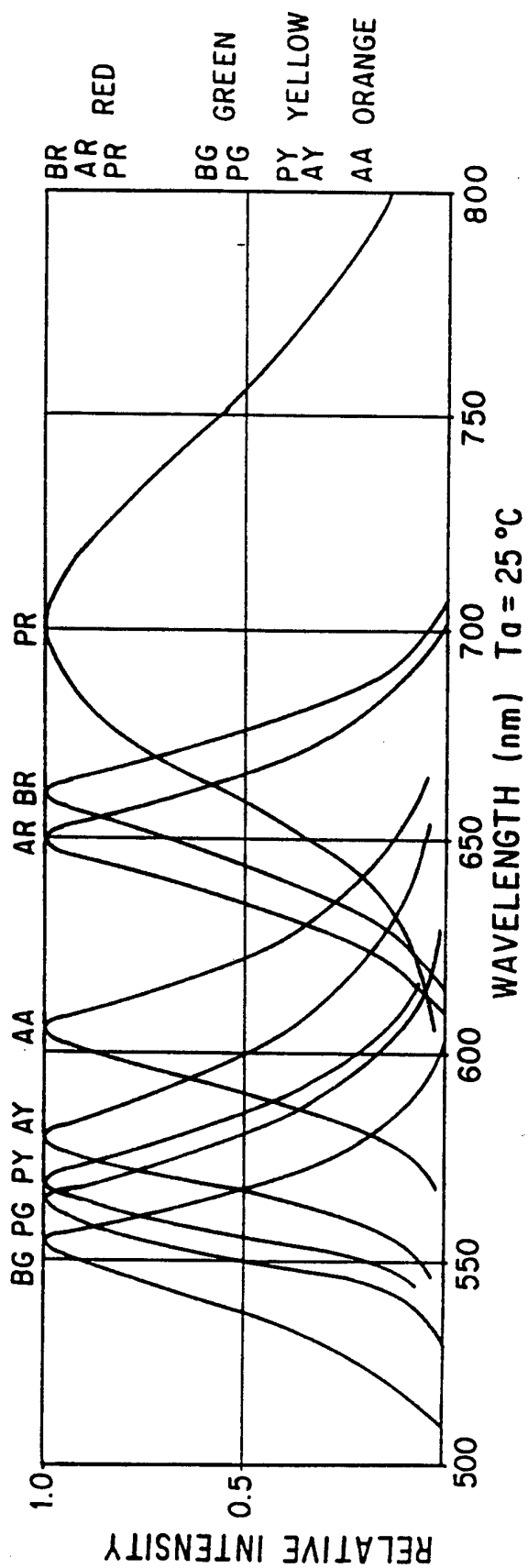


FIG. 6A

7/9

(COLLECTOR)
RELATIVE SPECTRAL SENSITIVITY
(EMITTER)
RELATIVE RADIANT INTENSITY

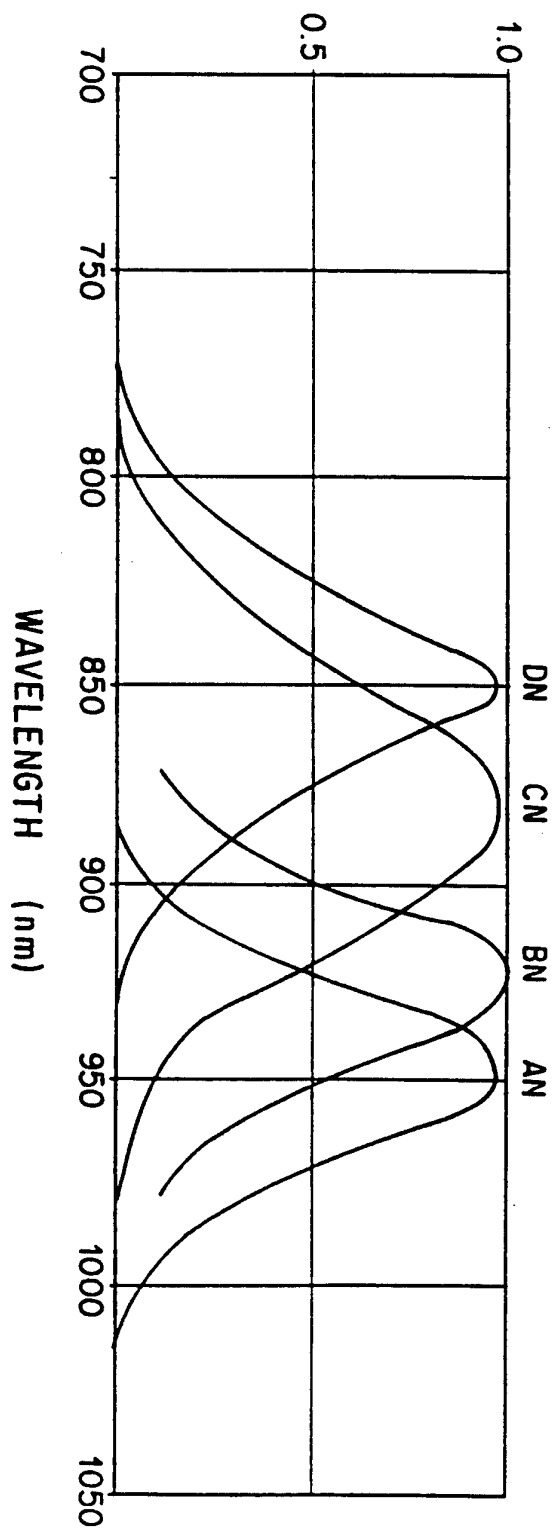


FIG. 6B

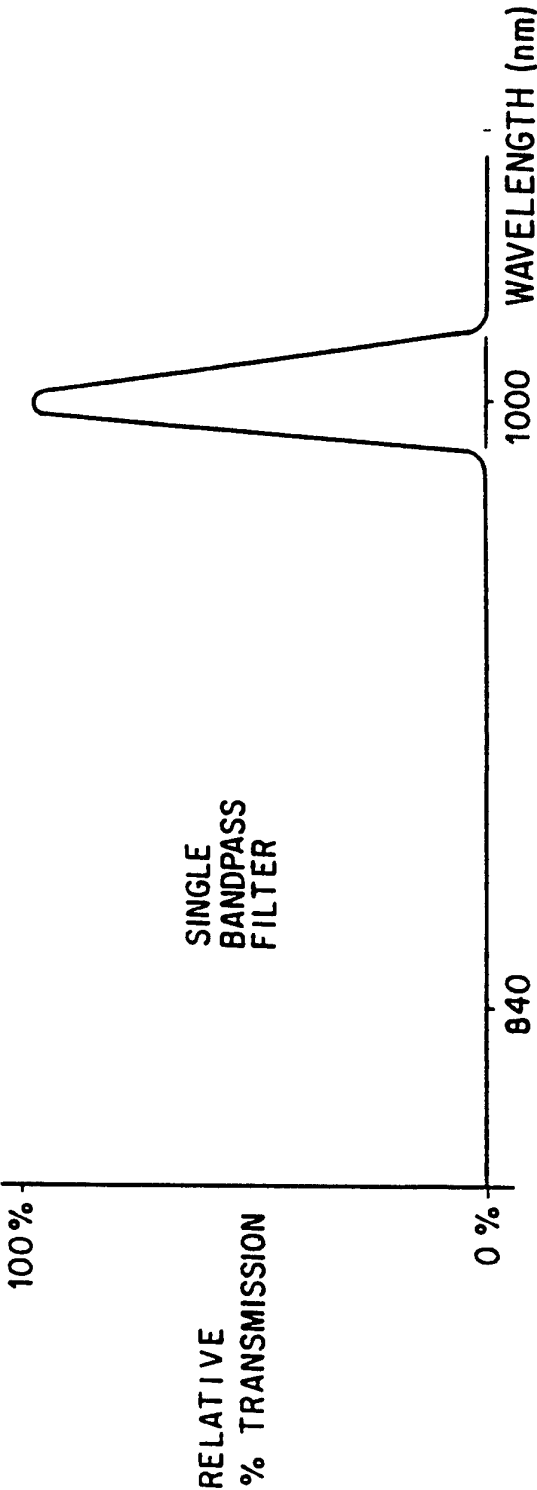


FIG. 7A

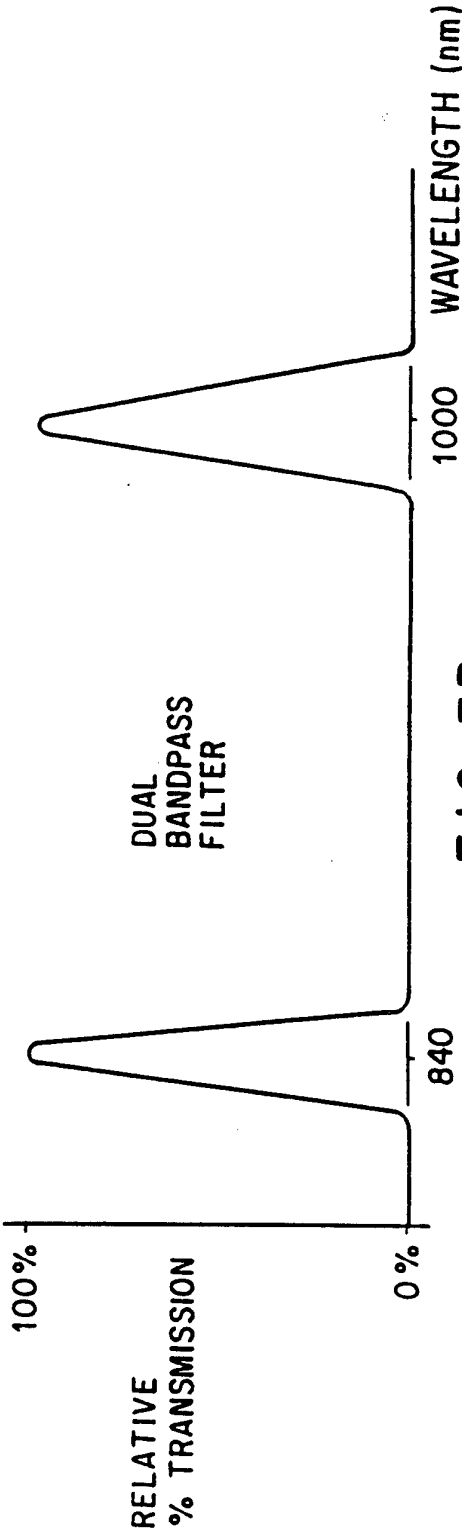


FIG. 7B

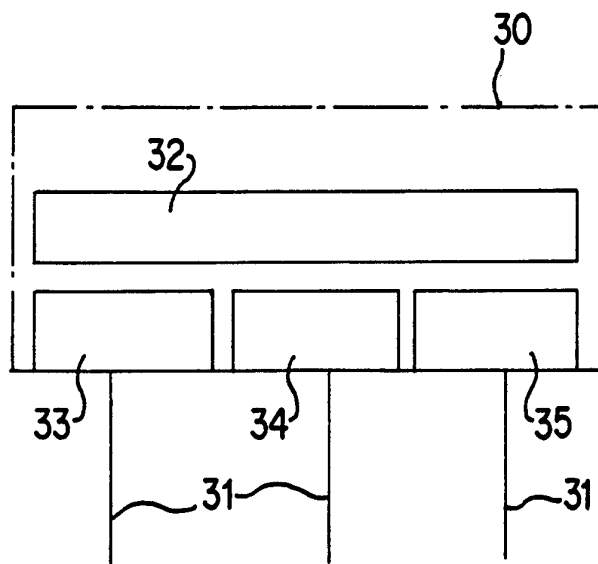


FIG. 8A

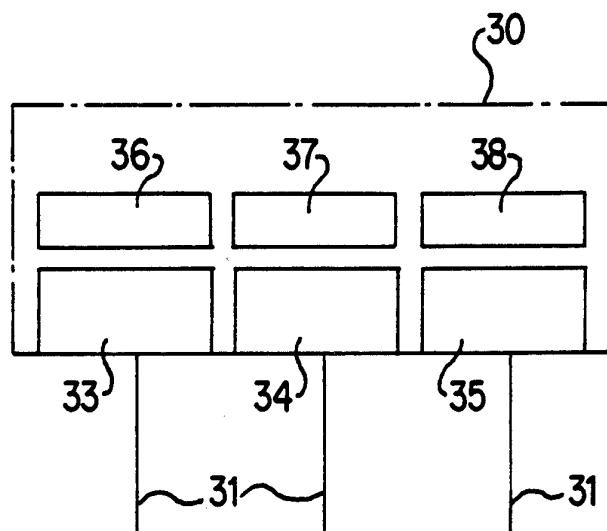


FIG. 8B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US93/06890

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :G01J 3/427

US CL :250/504R, 495.1, 338.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 250/504R, 495.1, 338.1, 494.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A, 4,620,104 (NORDAL ET AL.) 28 OCTOBER 1986. See entire document	1-12
A	US,A, 4,742,235 (KOJI) 03 MAY 1988. See entire document	1-12
X/Y	EU,A, 0,426,358 A1 (Yanger et al.) 08 May 1991. See fig. 1 and col. 5, lines 21-24	1, 12/2-4



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Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

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Authorized officer

KIET T. NGUYEN

Telephone No. (703) 308-4855