

Near infrared spectroscopy past and future

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I wish to dedicate this presentation to Tomas Hirschfeld (Picture 1). Before his untimely death almost ten years ago, Tomas was known as a founder of both Fourier transform mid-infrared and FT-Raman spectroscopy. When we joined forces back in 1979 to work on near infrared, one of the goals of his fertile and creative mind was to create the structure for the acceptance of near infrared spectroscopy among traditional mid-infrared spectroscopists residing in both industrial and academic communities around the world.

Foretelling the future in science reminds me of a passage from Lewis Carroll's "Alice Through the Looking Glass," where the Queen admonishes Alice to believe in impossible things. The Queen says to Alice: "when I was your age I always did it for half-an-hour a day. Why, sometimes I've believed in as many as six impossible things before breakfast."

The Queen in the story of "Alice" was right. If you want to predict the *distant* future in science, a hundred years from now, think of some impossible things and they are likely to come true so long as they don't violate the laws of thermodynamics. Let me give you an example of one such "impossible" discovery which has profoundly affected all of our professional lives, our



Picture 1.

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non-professional friends and their families. In two years we shall be celebrating the hundred year mark of the discovery of the electron, without which we could be having no meeting today. If you think of all the marvelous inventions connected to electricity that have derived from the discovery of the electron by J.J. Thompson in 1897—less than a hundred years ago—you can appreciate why I am so hesitant to forecast the distant future. As sure as we are here together, another remarkable discovery, this time no doubt in some other area of science, will throw all modest predictions to the wind. Therefore, I will stay away from the *distant* future and confine my remarks to the shorter span of the next 10 to 15 years, a safer and more realistic endeavor. Should some remarkable discovery occur during that time frame, it is unlikely to reach commercial proportions until the after this time, thereby providing a safety margin to the predictions that I will make today.

Incidentally, for those of you interested in an estimate of the commercial worth of the electron, the world's production of electronic equipment is now approaching an annual rate of one terabuck, i.e. one trillion dollars. Clearly, this would not have been predicted a century ago.

It is now a quarter century since the first commercialization of modern near infrared (NIR) analysis. At that time, FT-IR was in its ascendancy and universities taught their students that the near-infrared spectral region was essentially useless. Let us examine the history of this “impossible” development to help project the future.

What is modern near infrared analysis? It is the synthesis of NIR spectroscopy, chemometrics and instrumentation. The first steps were taken by Karl Norris and his staff at the United States Department of Agriculture Instrumentation Research Laboratory in Beltsville, Maryland. It was subsequently nurtured by the engineers and applications scientists at pioneering instrumentation companies and further developed by an increasing body of users around the world.

Karl Norris's first use of multiple linear regression to calibrate measurements using four visible wavelengths was the beginning of the symbiotic relationship between NIR technology and the calibration technology that was later named “chemometrics”. The result was the Internal Quality Analyzer built by Neotec to measure chlorophyll in fruits (Picture 2). Karl is shown here with Gene Gansel of Neotec. Near infrared spectroscopy was added in a later project for the purpose of measuring moisture in ground wheat by diffuse transmission.

As Karl was making NIR measurements of moisture in grains and oil seeds, he observed that the moisture errors were related to the protein and oil content. Recognizing that any effect causing



Picture 2.

a consistent error in another measurement can itself be measured, he proceeded to develop multiple linear regression calibrations for protein and oil also. In this same time frame it became known that carbon tetrachloride, used to reduce the scattering loss in the diffuse transmission measurement, was a carcinogen which could no longer be used. As an alternative, Karl experimented with the measurement of moisture in grains and oil seeds using NIR reflectance. The first prototype NIR reflectance instrument is shown in Picture 3.

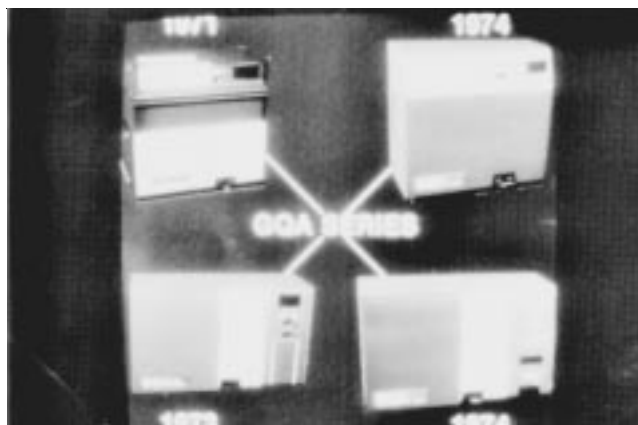
The first commercial instruments were developed to measure soybeans under contract to the Illinois Department of Agriculture 25 years ago by Neotec and Dickey-john, using the approach developed by Karl Norris at the Beltsville laboratories of the USDA. The Dickey-john GAC I instrument, shown in Picture 4, with Gordon Ropp, the Illinois Commissioner of Agriculture and Jim Anson, the Dickey-john Chief Engineer, used a rotating filter wheel to select six wavelengths for analysis. These wavelengths, selected by Karl, based on spectroscopy, are still in use today. In the original GAC I the calibration coefficients were set by soldering in appropriate value resistors. An early improvement was the introduction of the 20 turn potentiometers for entering the



Picture 3.



Picture 4.



Picture 5.

calibration constants. The Neotec GQA I instrument, at the upper left in Picture 5, used tilting-filter technology developed by the USDA to provide three short wavelength scans. The GQA I had potentiometers for the calibration constants but factory hardwired wavelength selections and filter standardization values. The “Delta OD” difference calculations used with the tilting filter technology were the forerunner of the ever more sophisticated data preprocessing techniques developed since. Both of these instruments depended on analog electronics as the microprocessor was not yet available. As too often happens when science mixes with politics, the project died when the Governor of Illinois was not re-elected. However, Neotec and Dickey-john continued to develop their series of instruments. In 1974, Technicon Industrial Systems joined with Dickey-john to market the first of the InfraAlyzers, the model 2.5, shown in Picture 6 being burned in before shipment.

At this time, Dr Philip Williams of the Canadian Grain Commission was running the busiest Kjeldahl laboratory in the world, performing 600,000 Kjeldahl analyses per year and incidentally



Picture 6.

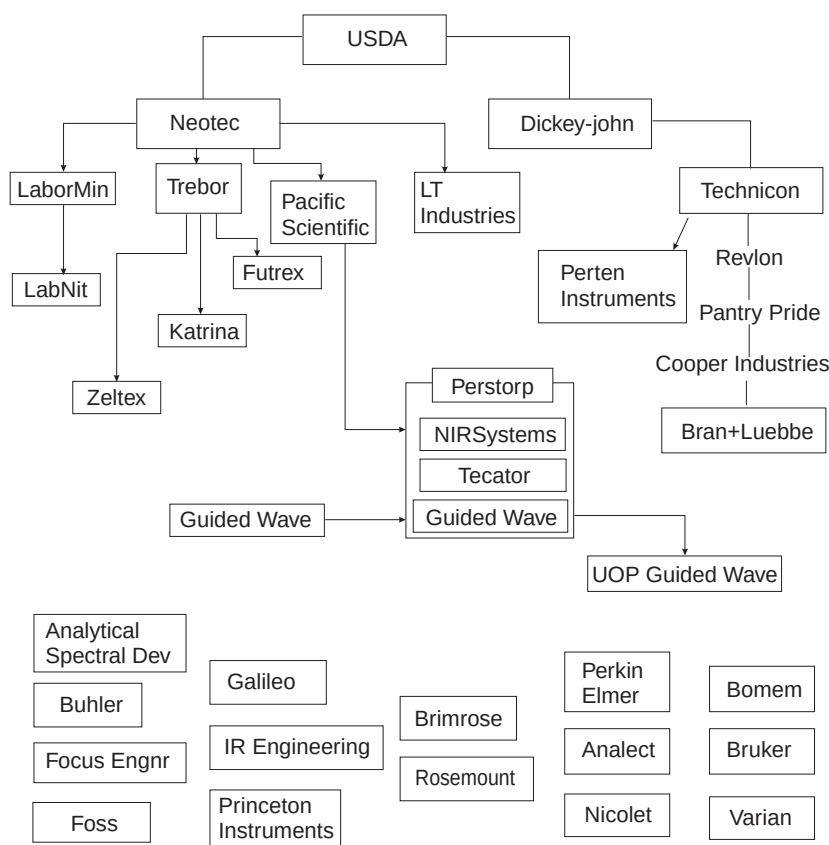


Figure 1. The “family tree” of NIR companies.

producing 47 tons of caustic waste in the process. Not being a politician, and based on real need, Phil took the risk of introducing NIR analysis in the marketing of wheat. In 1974 he specified and purchased the Automated Digital Analyzer (ADA) instrument from Neotec for \$96,000. From then until its retirement to a museum in Ottawa in 1993, the ADA ran without a breakdown 24 hours a day, 7 days a week to perform over 11 million tests for protein and moisture in wheat. This one-of-a-kind instrument saved \$250,000 in its first year of operation. Now NIR testing is saving the Canadian Grain Commission 2.5 million dollars per year.

As late as 1987, Williams and Norris listed only seven companies selling NIR instruments (Figure 1). What was the genesis of this expansion? In the beginning, Technicon marketed the Dickey-john model 2.5 and then went on to independently develop the InfraAnalyzer product line. A similar integrating sphere and rotating filter wheel technology was adopted by Perten Instruments. In Hungary, Labormim first licensed the Neotec designs and then developed its own instruments. In this country, Trebor and LT Industries were established by former Neotec employees. During the decade of the 1980s, both Neotec and Technicon, then the leaders in the field, went through a series of acquisitions. Neotec was purchased by Pacific Scientific and then changed its name to NIRSystems when it joined Tecator and Guided Wave in the Perstorp organization. Technicon retained its name as it was acquired in turn by Revlon, Pantry Pride and Cooper

Industries. Then Cooper sold the Technicon Industrial Systems portion to Bran+Luebbe. Since 1987 more than a dozen additional companies have entered the field, most of which have survived albeit many of them in relatively small niche markets.

What prompted this proliferation of NIR instrument companies? New companies have been formed as direct entrepreneurial spin-offs from existing NIR companies, as well as the entrance of established instrumentation companies into the NIR market. I predict this trend will continue, particularly in new areas such as medical, biological and environmental applications. However, with the entry of new players there will also be a simultaneous consolidation of the existing players.

What are the bottlenecks between research and the further development of NIR technology? First, the spectroscopy of NIR is difficult, being based on complex overtones and combinations of the fundamental vibrational bands of the mid-infrared. As Peter Griffiths has reported, detailed band assignments are essentially impossible for any but the simplest molecules. Pure simple chemical compounds are not a requirement for NIR analysis. In fact, one of the major advantages of NIR is the direct measurement of complex matrices without sample preparation, purification or separation. This technology allows us to choose between various measurement configurations, such as diffuse reflection, diffuse transmission and transflection, as determined by the application matrix and/or the sampling conditions. This flexibility can complicate the spectral data, thereby increasing the difficulty of spectral interpretation. As Hirschfeld pointed out in 1982, it is this spectroscopic complexity which provides the richness of the spectral information content on which NIR analysis operates. However, this is also “Why NIR is so hard to believe” (Figure 2).

Chemometrics follows spectroscopy as the second cornerstone of the NIR analytical technique. NIR has been a major vehicle for the development of chemometric calibration technology, including the introduction of partial least squares (PLS) by Martens at the Seventh World Cereal and Bread Congress at Prague in 1982. Chemometrics made NIR analysis different and therefore difficult for traditional spectroscopists to accept, as illustrated by Hirschfeld (Figure 3).

Now, other spectroscopies have adopted multiple linear regression (MLR), principle component regression (PCR) and partial least squares (PLS), the chemometric tools pioneered by the quantitative NIR community. This acceptance of computerized data analysis using statistical modeling techniques has now extended to qualitative analysis, particularly material identification in the pharmaceutical industry. Most recently, neural networks have become the focus of chemometric calibration research, with particular emphasis on non-linear calibrations. These multivariate calibration techniques allow the correlation of physical parameters, as well as

- No isolated peaks, just baseline wriggles
- Intensity is 1000x times down from middle IR
- Everything overlaps
- Spectrum interpretation is only an afterthought
- Spectrum fluctuations are much larger than extreme analytical change
- The computer picks wavelengths, interpretation procedure and calls out results that we cannot see at all in the data

Figure 2. Why NIR is so hard to believe (T. Hirschfeld 1982).

- Little or no sample preparation
- Analytical wavelength verification, not choice
- Unpredictable correlations may be useful
- Dependence on reference set
- Computer dependence
- Heavy computation load
- Secular constancy assumption

Figure 3. What's different about NIR (T. Hirschfeld 1982).

chemical composition, to spectral data, thereby providing the basis for applications such as octane number of gasoline, a measurement widely utilized by the petroleum industry.

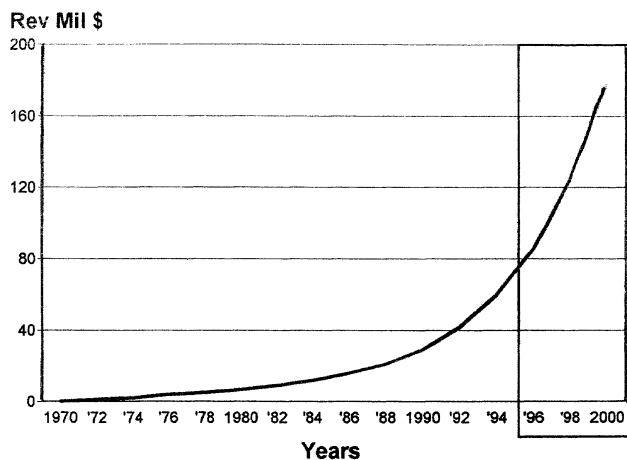
In the past, many users have accepted results without explicit understanding of the process of calibration and validation of the NIR method. The ASTM committee E-13 formed a task group on NIR over 10 years ago to provide standard practices in NIR. This group has now changed its name to the Chemometrics subcommittee, E-13.11, chaired by the author. It continues to have the responsibility for near infrared applications and for low-resolution NIR instruments whose methods are based on chemometric techniques. This year the "Standard Practice for Infrared, Multivariate, Quantitative Analysis" was fully approved and published as an ASTM Standard. This standard practice makes a significant step forward in specifying the important steps in calibration and validation. The subcommittee is currently developing standards appropriate to multivariate qualitative analysis, reference materials for reflectance level, wavelength and general instrument testing.

However, the "Limitations of NIR" analysis listed by Hirschfeld in 1982 still apply (Figure 4).

The advantages of NIR spectroscopy far outweigh these limitations where repetitive analyses are required, resulting in a rapidly growing instrumentation market. The estimated NIR instrumentation revenues (Figure 5) are projected to reach \$100,000,000 annually by 1997. The present compound growth rate of approximately 20% per year indicates that modern NIR technology has attained scientific and commercial acceptance. This 25 year long acceptance period after introduction is not unusual for new technologies. The estimated total revenues from 1970 thru 1995

- Methods development is slow
- Not suitable for trace analysis
- Spectroscopic experience not useful
- Non-casual correlations require extra precautions

Figure 4. Limitations of NIR (T. Hirschfeld 1982).



Year	70	72	74	76	78	80	82	84	86	88	90	92	94	96	98	00
Est rev. (\$M)	0	1	2	3.9	5.1	6.8	9.0	11.9	15.8	20.8	28.8	41.4	59.7	85	124	178

Figure 5. Estimated NIR \$ revenue.

(Figure 5) are 452 million dollars. At the present growth rate, the total would more than double in the next four years, reaching the cumulative billion dollar mark by the turn of the century.

This rosy economic scenario must be balanced with an important word of caution. The growth of any technology is fueled by both industrial and academic research and development. One indicator of the extent of such research is the number of publications appearing in the literature. The number of publications found in the annual searches of the bibliography provided and updated by the Council of Near Infrared Spectroscopy peaked at over 1100 articles in 1991. Unfortunately, it has fallen dramatically from 1992 through 1994 (Figure 6). In the absence of extenuating circumstances, this would lead one to predict that the technology has matured and the future growth rate will diminish substantially. It is true that the technology has matured to the point where papers simply reporting the determination of a new analyte are rarely being published. A second possible explanation lies in where the new applications are being done. Most of these are in the industrial arena where information is held as confidential and proprietary as a matter of standard operating procedure unless and until patents are issued.

Conference papers provide another measure of research and development activity. Tomas Hirschfeld and I jointly presented the only NIR paper at the 1981 Pittsburgh conference. By 1983, there were 12 papers in three sessions at FACCS. Although most of these papers concerned food and agriculture, they included the first paper on pharmaceutical product identification by J.R. Rose of Squibb and an early process control paper by R.D. Benson of Cargill. Further examination of the number of NIR papers presented at the Pittsburgh conference (Figure 7) shows a steady growth up to the 1992–1994 level.

The number of half day sessions (not individual papers) primarily devoted to NIR remained constant at four per Pittsburgh conference with about 45 papers being presented each year. In

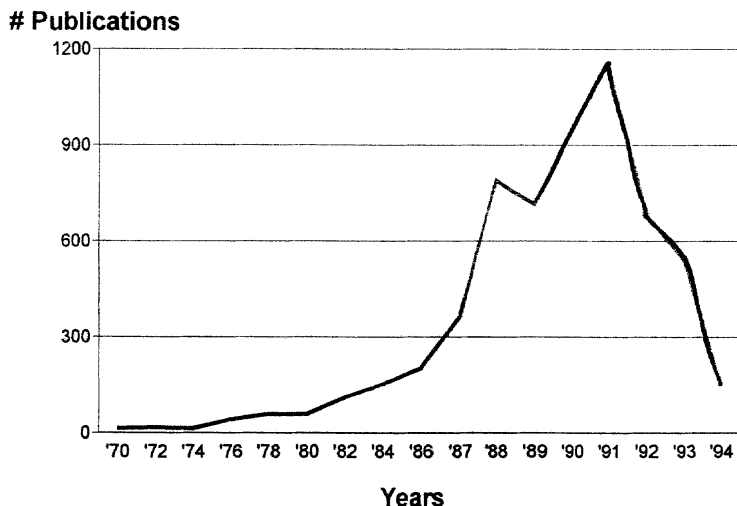


Figure 6. # of CNIRS bibliographic citations.

1995, many of the approximately 39 NIR papers were presented during the Process Analytical Chemistry Institute. This shift reflects the major increase in process oriented applications of near infrared spectroscopy.

During this same period the Eastern Analytical Symposium grew rapidly as *the* conference for NIR papers, with about 60 presented papers and posters in both 1993 and 1994. Based on these statistics, it appears that NIR is holding its own in a period of resource retrenchment for many areas of scientific research.

Application growth is based on both increased use of existing applications and the addition of new ones (Figure 8). From its beginnings as a method for determination of protein, oil and moisture in grains and oil seeds, the expansion of NIR spectroscopy has been fueled by new applications. First came food processing, feeds and forages and other agricultural applications. These were followed in the late '80s and early '90s by pharmaceutical, polymer, petroleum and chemical and the beginning of significant textile applications. Based on present research directions, I believe that environmental, biological and medical applications will become significant, and indeed major, contributors by the turn of the century.

I project that medical applications will be a major future growth area for NIR technology. Non-invasive *in-vivo* determination of blood glucose levels for control of diabetes is presently being researched by as many as 60 teams worldwide. Two companies have announced products, although regulatory approval remains to be obtained. The medical cost of diabetes and its complications is over twenty billion dollars annually and a recent nine year study by the United States National Institutes of Health showed that this cost could be reduced to one-half by tight

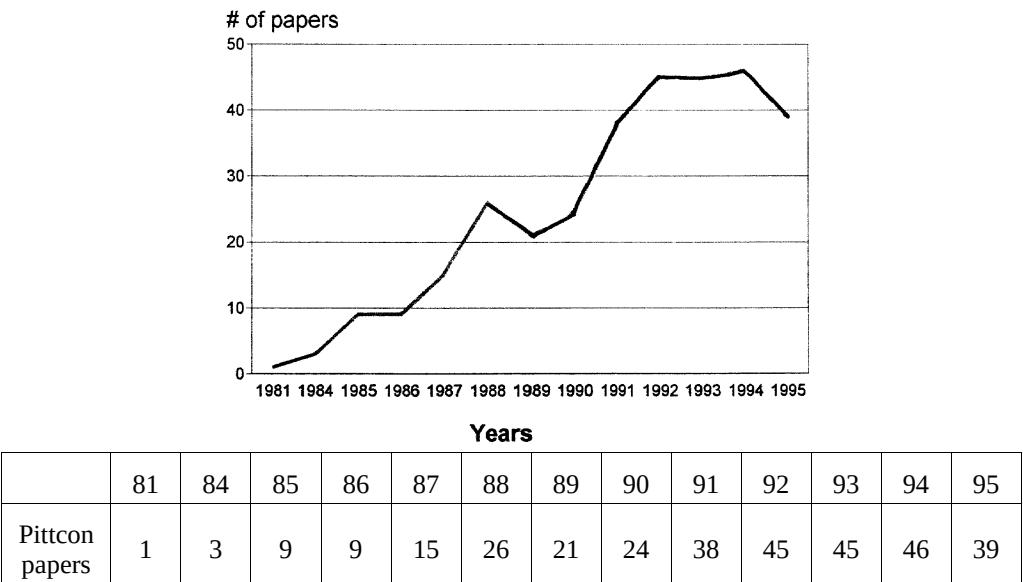


Figure 7. Near infrared Pittcon papers.

control of blood glucose levels. This is indeed a worthy goal for NIR spectroscopy combined with chemometric calibration.

A major medical use of very-near infrared (VNIR) spectroscopy, albeit a simple two wavelength measurement, is pulse oximetry. The oxygen saturation of the blood is determined non-invasively by NIR absorption of oxyhemoglobin. Monitoring oxygenation of the brain during anesthesia by non-invasive NIR spectroscopy is the goal of several research groups. Here depth

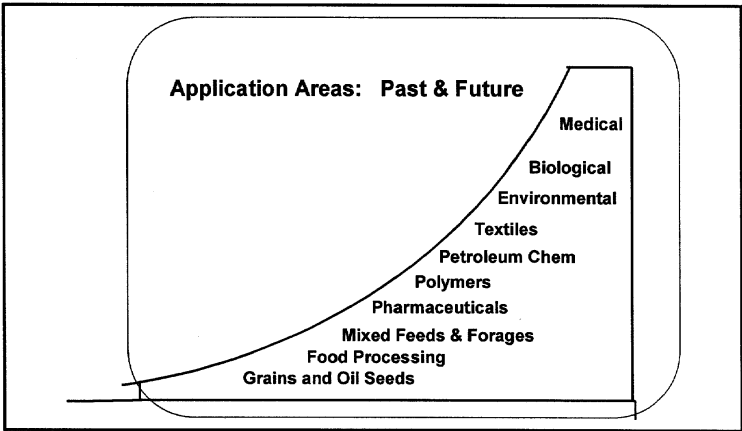
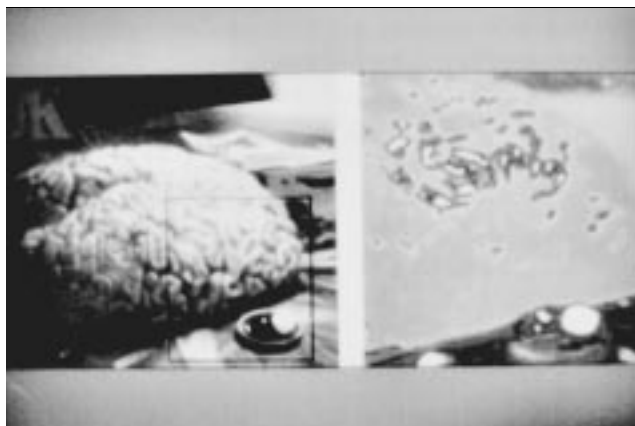


Figure 8.

profiling is of major importance. Time-of-flight measurements using picosecond laser pulses and depth detection based on radio-frequency modulation of the energy are two approaches being researched for this purpose. I predict that this NIR application will become routine in the operating rooms of the 21st century.

Dr Robert Lodder at the University of Kentucky and Drs Lewis and Levin at NIH are leading the medical use of NIR imaging. Dr Levin uses a microscope with a diode-array camera and AOTF for spectral selection. Dr Lodder is using NIR focal plane array cameras with a tunable laser for illumination and spectral selection. The laser provides an abundance of NIR energy at a rate of about 10 wavelengths per second. In earlier work, filters were used for spectral selection to produce the NIR images shown. Picture 7 shows the brain of a deceased Alzheimer's patient and adjacent to it is the NIR image of lipid and beta-amyloid concentration using six wavelengths. This image was created by a 4096 element (64×64 pixel) InSb focal plane array camera with 4096 intensity levels (12 bit). Each wavelength required 8 seconds for recording the filtered image and the blackbody energy used as reference. The black and white marbles provide additional optical and geometrical reference information. The information rate is of the order of 2 megabits per second. Picture 8 was made using the same camera during an endarterectomy operation during which the carotid artery is opened and the walls cleaned of lipid buildup. Here the NIR is measuring *cis*-, *trans*- and saturated lipids with 2–4 mm depth penetration in the 1725–1775 nm region. A surface total lipid measurement is made at 2310 nm.

These images led me to consider how a high-resolution imaging spectrometer might be constructed based on presently feasible components. An image size of 128 by 128 elements and a dynamic range of 16,384 : 1 (26 microabsorbance noise at unity reflectance) were chosen to assure a high quality image and sufficiently low noise to allow accurate characterization of the composition of the material being imaged using PLS or PCR calibrations and discriminant analysis. A spectral range of 5900 to 11,000 cm^{-1} (1695–909 nm) was selected, based on the region of optimum penetration into tissue and the spectral response of InGaAs detectors. Our earlier work on hydrocarbons¹ showed that a spectral resolution of 32 cm^{-1} (9.2 to 2.6 nm) was adequate for accurate determination of the composition of mixtures containing spectrally similar materials such as the isomers of xylene, toluene and benzene. A measurement time of less than two minutes is desirable, with shorter times being usable at reduced resolution or lower dynamic range.



Picture 7.



Picture 8.

Analysis of these specifications indicates that an imaging FT-NIR spectrometer can be conceived that meets these requirements. The system would be based on an 8 mm square 128×128 picture element InGaAs focal plane array similar to the existing liquid nitrogen cooled InSb arrays. The sample would be imaged onto the array allowing, for example, imaging a 1.6 cm square sample area with a spatial resolution of $125 \mu\text{m}$. The sample would be illuminated by energy from a conventional FT-NIR interferometer, such as the Bomem MB160, using a tungsten source and operating at a rate of two double-sided scans per second.

An interferogram would be generated for each picture element by sampling each pixel at 2148 samples per second. Considering scan efficiency, this results in a combined data rate of about 35 million samples per second. Dividing the array into 16 sub-arrays allows use of a presently available high speed 14 bit A/D converter such as the Analog Devices AD878 to digitize each of the 16 channels of information. Processing the data requires co-addition of, at most, 160 interferograms to achieve a digitizing noise limited dynamic range of $16,384 : 1$, indicating a maximum data acquisition time of 80 seconds for a complete image with full spectral data for each resolution element. Gain ranging may reduce the digitizing noise by a factor of up to 10 if the detector signal to noise ratio is much greater than $16,384 : 1$. Based on the MB160 source parameters and reasonable assumptions concerning the InGaAs array, it can be believed that a measurement time of less than 20 seconds might be achieved with the specified resolution and dynamic range. In that case a $4096 : 1$ dynamic range (12 bit) image, such as Lodder has shown, would require less than two seconds measurement time. Fourier transformation of the resulting interferograms is required to produce spectra. A single Analog Devices AD21060 SHARC digital signal processor can perform the required 1024 point FFT in 460 microseconds providing a data processing time of 7.5 seconds for the entire array of 16,834 elements. Parallel SHARC DSP units could further reduce this time. I predict that NIR spectral imaging instrumentation of this nature, that provides full spectral data for every resolution element, will be an important contributor to medical as well as other NIR applications development by the early years of the 21st century.

So, where have we been and where are we going? In the early 1980s NIR was almost exclusively used in food and agriculture as Hirschfeld summarized in Figure 9.

Tomas also suggested “Where NIRA Should Go” in 1982 (Figure 10).

The value of these suggestions is demonstrated by the extensive use of NIR spectroscopy in most of these application areas.

- **Grains** (protein, oil, moisture, starch, starch moisture)
- **Meat** (protein, fat, moisture)
- **Milk** (protein, fat, total solids, lactose)
- **Cheese** (protein, fat, moisture)
- **Fish meal** (protein, fat, moisture)
- **Feeds** (protein, carbohydrate, fiber, moisture, “nutritional value”)
- **Sugar beet** (sucrose, reducing sugar, fiber, type, amino acids I, smut, unsaturation, ash)
- **Flour** (protein, starch, protein type, ash)
- **Potatoes** (protein, starch, starch type, moisture)
- **Butter and margarine** (oil, moisture, unsaturation)
- **Nuts** (protein, oil, moisture)

Figure 9. Where NIR is (T. Hirschfeld 1982).

“Where NIR Spectroscopy Will Go?” next can be projected with some confidence. Medical and biological applications will include both quantitative, for example non-invasive blood and tissue analysis, and qualitative, such as invasive identification of arterial plaque material applications. NIR imaging will provide the surgeon with additional on-site information. This will become a routine procedure in the operating room. Environmental monitoring and waste management will become increasingly important. The sorting of waste materials, particularly plastics, for recycling is already being developed and will be further utilized. Pharmaceutical applications will move from the lab to on-line processing and product release as the regulators gain confidence in NIR capabilities. Textile fiber quality measurements, particularly for natural fibers such as cotton and wool, will increasingly utilize NIR technology to replace less precise and more labor intensive methods. Of course, NIR applications will continue to expand where NIR has already been, with a major shift to the real-time, in-line, process control application.

“How Will We Get There?” The three supports of this technology are spectroscopic understanding, chemometrics and physical instrumentation. Present research in multi-region correlation promises to aid our knowledge of the spectroscopy in all regions, but particularly of the difficult near infrared region. Near infrared spectral features will be assigned with more confidence based on their correlation with known features in other spectral domains.

- **Gasoline** (aromaticity, lead, paraffins, naphthenes, *t*-butylalcohol, benzene, toluene)
- **Oil shale** (kerogen)
- **Crude petroleum** (paraffins, naphthenes, sulfur)
- **Clays** (type, moisture)
- **Explosives and propellants** (components, F/O ratio, binders, fillers, moisture, wax)
- **Composites** (binders)
- **Textiles** (Fiber types, sizing, moisture)
- **Pharmaceuticals** (most major constituents)
- **Latex** (hydrocarbons, detergent, particle size)
- **Skin** (moisutre, fat, disease states)
- **Wood** (moisture, preservatives, lignin)
- **Leather** (protein, fat, moisture, tanning agents, cross-linking, hydrolysis)

Figure 10. Where NIR should go (T. Hirschfeld 1982).

Currently used chemometric techniques tend to be soft-modeling methods which attempt to extract information from the spectral data without utilizing *a priori* spectroscopic or instrumentation response function knowledge. The neural network is a prime example of such techniques. This, in my opinion, is a serious limitation. However, neural networks do appear to be potentially useful for non-linear situations. I look to the future to pay greater attention to utilizing *a priori* information inherent in the measurement hardware and sample. Data pretreatments to minimize unnecessary variability in the data and inclusion of additional parameters in the model that are derived from measurements made by other techniques, will enhance and enlarge the performance of NIR analyses. Progress will be made in calibration optimization techniques such as determination of optimum weighting factors for data at each wavelength.

Finally, instrumentation will continue to improve. Instrument standardization techniques will be developed so that calibrations will be transferable among instruments, at least those of similar design, without the need for extensive transfer sample sets. The information rate produced by instruments will increase to meet the needs of real-time applications. Full-spectral imaging places the most demanding requirements in this area, requiring recording of millions of data points per image to provide both spectral and spatial resolution. Real-time applications may require tens of spectrally resolved images per second. As additional types of samples and measurement conditions are encountered, new sample interfaces will be developed to meet these changing requirements.

The last quarter century of development of NIR spectroscopy has been an exciting time. “The Future Waves” us on to meet new challenges in the implementation of this important technology.

Reference

1. E. Stark, “Near Infrared Spectroscopy: The New FT Frontier—Spectroscopic and Chemometric Considerations”, *SPIE Vol. 1575*, 8th International Conference on Fourier Transform Spectroscopy, pp. 70–86 (1991).