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One Hundred Years of Progress in Food Analysis

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Food and agricultural products comprise complex and diverse chemical mixtures that historically have presented challenges for assessing food safety, nutrient content, stability, and sensory qualities. The analysis of food composition has significantly evolved over the past 100 years, progressing from reliance on predominantly "wet chemistry" laboratory methods from the early to mid-20th century to their gradual replacement by modern instrumental techniques. Pioneering developments in pH instruments, spectrophotometry, chromatography/separations, and spectrometry often had immediate applications to food analysis. Continuous improvements in methodology over this period have led to significant enhancements in analytical accuracy, precision, detection limits, and sample throughput, thereby expanding the practical range of food applications. The growth and infrastructure of the modern global food distribution system heavily relies on food analysis—beyond simple characterization—as a tool for new product development, quality control, regulatory enforcement, and problem-solving.

KEYWORDS: Analytical methods; characterization techniques; food analysis; food products; separation techniques; chromatography; mass spectrometry; spectroscopy

INTRODUCTION

From a chemical perspective, food is an intricate, heterogeneous mixture of diverse biochemical components. Analytical food chemists are concerned with the composition and properties of food products, beverages, confections, and flavors including the chemical and physical changes they undergo during postharvest handling, processing, and storage. Measuring the quality, safety, sensory properties, nutrition, and stability of food products is the primary concern of analytical chemists working within the food-processing industry and in academic and government laboratories affiliated with food science or testing programs.

Food assays have been developed to enable measurement of food product quality attributes (appearance, color, flavor, texture), depending on the specific product application. Alternatively, the instability of foods, which limits their shelf life, can be initiated by chemical reactions, enzymatic reactions, microbial tranformations, or physical forces. Analysis of the degree of emulsification or moisture content, for example, may allow a prediction of the shelf-life limit for a salad dressing or a snack cracker, respectively. Analysis of food pigments concerns darkening, bleaching, or development of desirable colors. Flavor assays measure oxidative rancidity, undesirable browning reactions, or desirable compounds produced through fermentation or thermal reactions. Texture assays evaluate toughening or softening, loss or gain in solubility or water-holding capacity. Besides quality assurance, the goals of food analysis may be directed toward basic research (healthy food ingredients, bioactive compounds for disease prevention) or product development (convenient preparation, improved sensory attributes).

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The chemical analysis of food composition has significantly advanced over the period from 1908 to the present and is the subject of recent comprehensive reviews and compendia of methods and instrumentation (*1*−*5*). As anaytical chemistry evolved over the same era (*6*), classical monographs and textbooks devoted to food analysis underwent multiple editions and revisions, many spanning several decades (*7*−*9*). In the United States, classical methods of food analysis were initially developed to provide reliable and reproducible information about food composition due to frequent incidents of food adulteration and the need for consumer protection. The early focus of food analysis was to differentiate levels of food components, assess purity, and expose economic fraud. As the science of food components evolved from 1900 to 1940 through subsequent discoveries and further understandings of the roles of vitamins, minerals, proteins, lipids, and other essential nutrients, the need arose for the development of analytical methods that could verify nutrient content. Early agricultural chemists were interested in providing links between food composition and nutrition, just as they are today.

New federal regulations were enacted in countries around the world, requiring commercially processed foods to be labeled to declare their ingredients (for example, in the United States with the Federal Food Drug and Cosmetic (FD&C) Act of 1938) and, subsequently, their nutritional value (U.S. Nutrition Labeling and Education Act of 1990.) Protein, vitamin A, and vitamin C are among the list of 14 nutrients required to be disclosed on the package label since 1993 (*10*), and this new regulation generated the need for more accurate analytical tests for trace nutrients in foods. In addition, more rapid analytical methods needed to be developed to allow food processors to declare levels of cholesterol and saturated fat in foods, rather than reporting total fat content. The requirement to declare *trans*-fat content on packaged food

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Table 1. Sources of Official Analytical Methods for Food Analysis

standard analytical methods	organization/publisher	food matrix/analyte
Official Methods of Analysis	AOAC International	foods, food additives, trace nutrients, animal feed
Approved Methods	American Association of Cereal Chemists (AACC)	flour, gluten, dough strength, starch, fiber
Official Methods and Recommended Practices	American Oil Chemists' Society (AOCS)	vegetable oil source materials: fatty acids, glycerides, glycerin, lecithin, *trans*-fats
Standard Methods for the Examination of Dairy Products	American Public Health Association	acidity, fat, lactose, moisture, protein, rancidity
Food Chemicals Codex	U.S. Pharmacopeia	preservatives, flavorings, colors, vitamins
TTB Methods	U.S. Alcohol Tobacco Tax and Trade Bureau (TTB)	alcohol, calories, protein, carbohydrates in wine, malt, distilled beverages

labels was added in 2006 to allow consumers to make healthier food choices to reduce their risk of coronary heart disease (*11*). Mandatory food nutrition labeling provided the impetus to develop new standardized methods for food analysis that could measure a broader group of components, particularly for complex matrices in multicomponent "prepared" food products. These new methods were essential tools for food processors in manufacturing and for government regulatory agencies in enforcement.

Standardized food analytical methods enable consistency of results among different laboratories that follow the same procedures and serve as a benchmark for comparing results in the development of new methods. Several nonprofit scientific organizations have compiled and published standard methods of analysis for diverse food products, which have been collaboratively studied and validated (**Table 1**). These include *Official Methods of Analysis* (*12*) published by AOAC International, an organization founded in 1884 to initially provide analytical methods for fertilizers, feeds, and dairy products to serve food chemists in government and regulatory agencies. Current methods cover a range of analytical tests across foods, food additives, beverages, and agricultural materials. The American Association of Cereal Chemists (AACC) publishes *Approved Methods* (*13*) for cereal products relating to baking quality, dough strength, staling, starch, fiber, and proximate tests (e.g., mosture, crude fat, protein). *Official Methods and Recommended Practices* (*14*) relating to fat and oil analysis are published by the American Oil Chemists' Society (AOCS) for oilseed components, lipid materials, and finished food products, in addition to soaps and detergents. The American Public Health Association publishes *Standard Methods for the Examination of Dairy Products* (*15*), which include methods for the chemical analysis of milk and dairy products (acidity, fat, lactose, protein, water content). *Food Chemicals Codex* (*16*) is a compendium of standardized analytical methods and tests for the purity and quality of food ingredients including preservatives, flavorings, colors, and nutrients. In the United States, the Alcohol Tobacco Tax and Trade Bureau (TTB) has developed official analytical methods (*17*) to measure alcoholic content, calories, protein, and carbohydrates in wines, malt beverages, and distilled alcoholic beverages.

As the global food industry continues to expand, food analysis plays an essential role in understanding and utilizing chemistry to measure food product stability, quantifying changes in flavor chemistry associated with sensory characteristics, determining the end of product shelf life, developing ingredient specifications, and problem solving in product development, production, and quality control. In addition, ensuring the safety of foods has become an international mandate for food processors and governmental agencies. In the United States, food safety implies the absence of pathogenic microbiological organisms in foods; however, it broadly encompasses the control and chemical measurement of pesticide, antibiotic, and mycotoxin (e.g., aflatoxin, fumonisin, ochratoxin) residues in animal feeds and foods. Because of increased incidences of foodborne allergies, the U.S. Food Allergen Labeling and Consumer Protection Act of 2004 required mandatory labeling of the eight major food groups that comprise 90% of allergenic responses (milk, eggs, fish, crustacean shellfish, tree nuts, peanuts, wheat, soybeans) (*18*). The need for fast, high-volume screening has driven the development of rapid analytical test kits. Two examples are those that employ enzyme-linked immunosorbent assay (ELISA) techniques (e.g., detection of wheat gluten and peanut protein allergens in processed foods) and monoclonal antibody-based affinity chromatography methods (e.g., assay of aflatoxins in peanuts, cereal grains, and milk). Today, as in the past, regulatory and food safety concerns compel the ongoing development of analytical testing methods to ensure food authenticity, monitor economic adulteration, and screen for the presence of chemical toxins and food additives to ensure compliance with local government regulations. Sophisticated analytical tools such as HPLC, near-infrared spectroscopy, site-specific natural isotope fractionation (SNIF)-NMR, and ^{13}C stable isotope ratio analysis−mass spectrometry are frequently used to verify authenticity of fruit juices, natural flavors, spices, essential oils, and other expensive food ingredients. (*19*−*23*).

FEDERAL REGULATION DRIVES NEED FOR FOOD ANALYSIS

Much of today's analytical food testing has its roots in food safety and the prevalence of economic adulteration in the early 20th century that ultimately led to the creation of the U.S. Food and Drug Administration (FDA) (*24*). A large part of the motivation for performing early food analysis was to protect consumers against fraud, such as unscrupulous food manufacturers adding alum or gypsum to flour, cottonseed oil to olive oil, or dried leaves to pepper (*25*, *26*). The FDA's origins can be correlated with the 1906 publication of Upton Sinclair's best-selling novel *The Jungle*, which described in graphic detail the filth and unsanitary practices then prevailing at the Chicago stockyards. The public's outraged response prompted the U.S. Congress to propose new legislation. In June 1906, President Theodore Roosevelt signed into law the Food and Drug Act, also known as the "Wiley Act" after its chief advocate, Dr. Harvey W. Wiley (*27*). This was the first federal law aimed at regulating interstate commerce of misbranded or adulterated foods, beverages, and drugs.

The Act prohibited, under penalty of seizure of goods, the interstate transport of food which had been "adulterated", with that term referring to the addition of fillers of reduced "quality or strength", coloring to conceal "damage or inferiority," formulation with additives "injurious to health," or the use of "filthy, decomposed, or putrid" substances. The Act applied similar

penalties to the interstate marketing of "adulterated" drugs, in which the "standard of strength, quality, or purity" of the active ingredient was not either stated clearly on the label or listed in the United States Pharmacopoeia or the National Formulary (*27*). The responsibility for examining foods and drugs for such adulteration or misbranding as part of the enforcement of this Act was entrusted to the Bureau of Chemistry headed by Wiley in the U.S. Department of Agriculture (USDA).

Interestingly, the foundation for the Bureau been laid 22 years earlier with the establishment in 1884 of the Association of Official Agricultural Chemists (AOAC) under the auspices of the USDA (*28*). Its key role at that time was to adopt uniform methods of analysis for fertilizers. In 1885, a convention establishing AOAC as an independent organization was held in Philadelphia, PA. Its membership was restricted to analytical chemists in state and federal government positions, a membership requirement that remained in effect nearly 100 years later.

The early years of AOAC were strongly influenced by Wiley, a founder of the association who served as its president and secretary. In 1885, Wiley oversaw the publication of the *AOAC Methods of Analysis*, a 49 page bulletin of chemical methods for the analysis of fertilizers. By 1887, the publication had grown to include methods for feeds and dairy products as well as fertilizers. Dr. Wiley's interest and concern for the adulteration of foods and drugs led to the study and adoption of official methods for foods in 1889, and by 1912 AOAC was publishing the *Official and Provisional Methods of Analysis*. This became the impetus for development of standardized and collaboratively tested analytical methods for food substances and ingredients, which were peer-reviewed at multiple stages in the methods development process.

In 1927, the Bureau of Chemistry's regulatory powers were reorganized under a new USDA body, the Food, Drug, and Insecticide Organization. This name was shortened to the Food and Drug Administration in 1930. Following the groundwork laid during the first part of the 20th century, food regulation in the areas of labeling, standard specifications, nutritional claims, and approved additives continues to influence and direct analytical methods development.

EARLY PERIOD (1908−1950): WET CHEMISTRY REIGNS

The typical food analysis laboratory in the early 20th century (**Figure 1**) appeared very different from modern food research and testing facilities. During this period, nearly all food analyses were performed using "wet chemistry" methods. A majority of these methods were designed to utilize chemicals and equipment that were readily available in typical chemical laboratories, such as glassware, weighing balances, Bunsen burners, and ovens. Typically, classical methods involved combinations of elaborate analytical procedures such as weighing, mixing, filtering, evaporation, distillation, or solvent extraction (*29*). The traditional practices of these wet chemical analyses were highly deductive. Clues to identifying substances and their levels arose from volume determinations, titrations, or precipitations, with the results judged by the subjective, if trained, eye of the food chemist. Physical methods of analysis—measuring light absorption or electromagnetic properties of food—almost inevitably found the food chemist connecting optical and electrical components with traditional glassware, ceramics, and rubber tubing.

The foundation for these methods had been laid in the 1800s with the development of assays used with synthetic organic chemistry and for characterization of natural products in food and feed. The contributions of early German and other European chemists to food analysis have been reviewed (*26*). Many of these early scientists developed chemical procedures for elemental analysis and isolation of organic substances that were later applied to the study of food composition. In 1842, Liebig attempted to classify foods on the basis of their chemical constituents and nitrogen content, whereas Henneberg devised an analysis scheme in the 1850s to determine proximate composition in a manner still used today (*30*). Moisture was determined by heat-drying; fat was extracted with diethyl ether; nitrogen content was converted into protein by applying a factor of 6.25; crude fiber was measured by its insolubility in dilute acid and alkali, from which residual ash and fat was subtracted; total carbohydrates were calculated by difference. The 6.25 conversion factor was based on an assumption that animal proteins contain 16% nitrogen, of which all is derived from protein (which we now know to be false). Overlaps between the nutritional sciences and agricultural chemistry provided early research on food composition, energy values of foods by calorimetry, and the digestibility and availability of food macronutrients from notable contributions by Rubner in Berlin and Atwater at the Storrs Agricultural Experiment Station in Connecticut in the early 1900s (*30*). Of historical interest is that a preponderance of synthetic organic and analytical chemistry advancements occurred in Germany prior to World War I, and early chemists received their training in Germany to learn these techniques up until World War II (*31*).

Several examples are representative of the development of early classical wet chemistry methods. In terms of its relative significance and impact on quality and safety, moisture determination is one of the most widely used measurements in the processing and testing of foods. However, accurate and precise moisture measurements are difficult to obtain, because the degree of water binding within a food product influences its ease of removal (*2*). Early techniques involved codistillation with a high boiling point solvent or use of drying ovens. The Karl Fischer titration (iodine reduction by SO_2 in the presence of water) developed early as the preferred method for the determination of water in low-moisture foods such as dried fruits and vegetables or foods high in sugar or protein.

The Kjeldahl measurement of protein (digestion with sulfuric acid and copper catalyst; boric acid titration of NH_3) became a standard food analysis technique for over 100 years (*2*, *3*). The Kjeldahl method's universality, precision, and reproducibility made it the internationally recognized standard method for estimating the protein content in foods. However, the Kjeldahl assay does not exclusively measure protein content. The assay's inability to differentiate protein from nonprotein nitrogen was exploited in two adulteration incidents in China (pet food, 2007; milk powder, 2008) when melamine, a nitrogen-rich chemical used in plastics and fertilizer, was added to the diluted food material to falsify high protein contents. Additional disadvantages of the Kjeldahl method, such as the need to use concentrated sulfuric acid at high temperature with a relatively long digestion time, led to the development of the Dumas nitrogen combustion method for measuring crude protein content. The Dumas method was developed in the 1940s, but it initially was not a practical routine analytical tool until the instrumentation was further developed and made more user-friendly in the 1990s. Instrumental nitrogen combustion methods (e.g., LECO) are becoming more frequently utilized to determine protein content, even though the microscale Kjeldahl method continues to be routinely used in food analytical testing laboratories at the present time.

Often, the reliability of classical food analysis methods is directly related to the skill of the analyst, an example being the determination of vitamin A and β-carotene in foods. The official analysis method is the Carr−Price assay, which was developed in 1947 and utilizes a colorimetric measurement at 620 nm to determine the analyte concentration (*32*, *33*). The reaction of antimony trichloride with vitamin A in chloroform yields an intense but unstable blue color. The reproducibility and accuracy

Figure 1. Analytical chemistry laboratory at the USDA Fixed Nitrogen Research Laboratory, near Washington, DC, in the 1920s (courtesy Chemical Heritage Foundation).

of the assay is highly dependent on the subjective interpretation of the color change by the analyst and the time interval at which the titration is performed after the sample extraction (*34*). In addition, the relatively strong acidic conditions can promote cis/trans isomerization of the native retinols. Because of other colored chemical interferences present in many types of food samples that can influence the accuracy of the results, colorimetric methods such as Carr−Price were eventually replaced in the 1980s by faster, more accurate high-performance liquid chromatography (HPLC) methods (*35*). In most cases, analytical food testing laboratories no longer perform vitamin assays using the earlier colorimetric methods, even though they remain the official methods.

The analyses of trace minerals (calcium, copper, iron, manganese, zinc) and toxic heavy metals (lead, cadmium, mercury) in foods were initially performed by wet chemical titration assays of precipitation complexes or reactions with chromogens to form colored products that can be quantified by light absorption (*2*). These techniques initially were replaced by the commercialization of atomic absorption spectrometry in 1963, followed later by inductively coupled plasma (ICP)−atomic emission spectrometry in the 1980s and ICP−mass spectrometry in the 1990s (*2*, *36*). However, even at the present time, the analysis of table salt (sodium chloride) in foods is routinely determined as chloride by titration with silver ions.

In the latter half of the 20th century, the time spent on such laborious and difficult wet chemical analyses began to decline. Although many classical methods are still widely used today, they were eventually substituted with instrumental methods that provided lowered detection limits, increased analyte specificity, simplified use, reduced cost, higher sample throughput, and automation capabilities.

EARLY INSTRUMENTAL DEVELOPMENTS (1930−1950)

The instruments utilized for food chemical analysis in the early part of the 20th century were quite crude. As an example, the Bishop electrotitrimeter was a device invented in the early 1900s for measuring the concentration and percentages of acid in substances (*37*). These early instruments were composed of fragile glassware, wires, galvanometers, and elaborate components, and considerable analyst time was expended in the construction and maintenance of these devices in the laboratory. The practical utility of glass pH electrodes would require advances in electronics capable of measuring high resistance values. In 1934, a significant milestone was achieved when Arnold O. Beckman designed his first electronic pH-meter, the "Acidimeter" (*38*). Beckman built the instrument as a personal favor for a former classmate who was working as a food chemist at the California Fruit Growers Exchange on a lemon byproduct. To maintain uniform product quality, it was necessary to measure the acidity of lemon juice, which correlated with its relative sourness. However, the chemist had considerable difficulty measuring the pH using a fragile, thin-glass silver/silver chloride electrode (to reduce resistance to small electrical currents) connected to a delicate galvanometer. One of these components was frequently breaking, and the electrical signals were weak. Beckman offered to fabricate the system himself, incorporating a thicker walled, more rugged glass electrode with an electronic amplifier using vacuum tubes to enhance the signal strength. The Acidimeter was such a success that other colleagues learned about it and asked if Beckman could build a few more. He immediately recognized the utility for food scientists to have a compact and portable instrument enclosed in a "black box" that was designed to be rugged in laboratory and processing environments. With that vision, Beckman ushered in a new era by forming a new company, National Technical Laboratories, to market the pH-meter, thus initiating the modern instrumentation industry and the early stages of the transformation of food analysis. The Beckman model G pH-meter introduced in 1937 following two earlier prototyes was the first commercial laboratory instrument to combine electronics

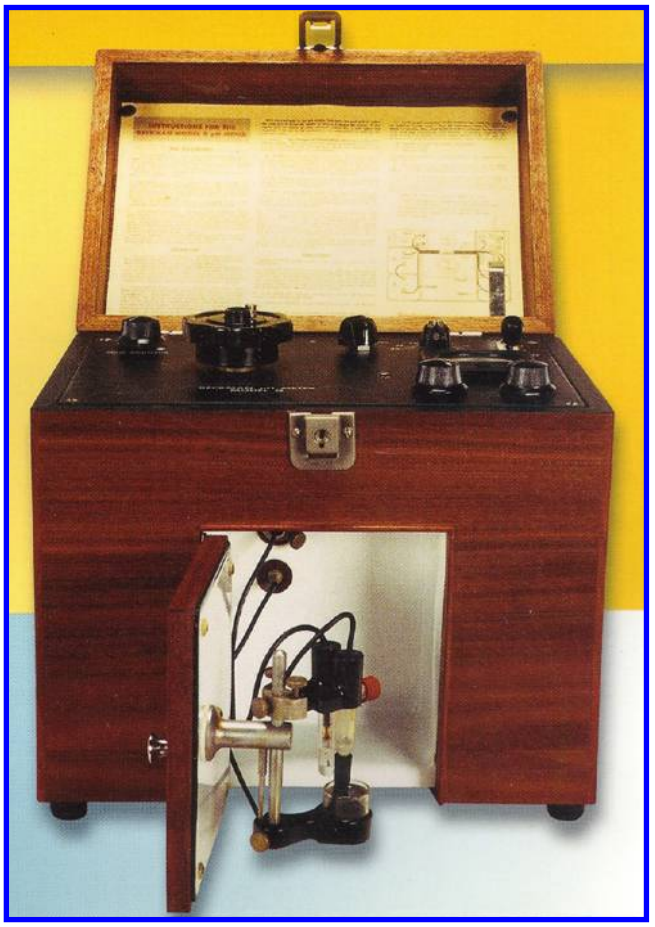

Figure 2. Beckman model G pH-meter (1937) (courtesy Chemical Heritage Foundation).

with direct chemical measurement (**Figure 2**). It demonstrated for the first time that instruments could eliminate the subjectivity, fragility, and complexity of earlier methods. To recognize its significance, the American Chemical Society designated the development of the Beckman pH-meter a National Historic Chemical Landmark in 2004 (*39*).

The next significant analytical instrument that Beckman developed of importance to food analysis was the model DU ultraviolet (UV) spectrophotometer (*38*). It used similar electronic technology that was designed for the pH-meter and was first marketed in 1941 by National Technical Laboratories (now Beckman Coulter). With the availability of commercial instrments, UV measurements became an essential component of every food analysis laboratory for various colorimetric assays, which related the intensity of solution color as a way to quantify concentration of a specific analyte. As previously discussed, colorimetric end points were typically used in vitamin assays.

Immediately before World War II, infrared (IR) spectrophotometers were under development by Beckman and others for the classified development of synthetic polybutadiene rubber and higher octane aviation fuel. IR spectrophotometers relied on an optical source, prisms, and electronics to detect the characteristic stretching vibration "fingerprints" of molecules produced by their interaction with IR light. The Perkin-Elmer Co. developed an early prototype model 12 IR spectrophotometer in the 1930s, which was further perfected before being sold in 1944 as the first IR spectrophotometer made commercially available to the scientific community (*29*). However, in 1951 Perkin-Elmer introduced its highly successful infrared spectrophotometer, model 21, which made IR a routine laboratory tool for food analysis. It was followed in 1957 by the model 137, a popular low-cost laboratory instrument. Infrared analysis proved to be more powerful than UV spectroscopy, because it provided chemical information about organic functional groups and structure elucidation. IR enabled new food components to be rapidly identified by comparison with known standards and to be analyzed for purity. Because IR anaysis is able to differentiate cis- versus trans-isomers, it is particularly useful in food lipid applications to assess the trans-content of unsaturated fatty acids in hydrogenated oils. IR (followed later by near-IR) analysis provided an early role in driving the shift from traditional wet methods to modern instrumental analysis. It demonstrated that direct objective measurement could be simpler, faster, less expensive, and considerably more accurate and precise.

PIONEERING ADVANCEMENTS IN CHROMATOGRAPHY

The development of chromatography within the past century has provided the broadest impact and largest application to the discipline of food analysis. Just over 100 years ago, a Russian botanist, Mikhail Tswett, invented liquid chromatography as part of his investigations on plant leaf pigments and first presented his findings in 1901 as the XI Congress of Naturalists and Physicians in St. Petersburg, Russia (*40*). Tswett's research led to the discovery of a liquid adsorption technique that permitted the separation of chorophylls and xanthophylls on a calcium carbonate adsorbent, with elution by petroleum ether/ethanol mixtures. In subsequent years, he further refined the technique, which in a 1906 publication he termed chromatography, or "color-writing", derived from the Greek words *chroma* and *graphikos* (*41*). In his application, the separation of chlorophyll leaf pigments was clearly visible as colored bands on the adsorbent column. Because his findings were published in the Russian technical literature, their applications were largely unknown by Western scientists and fell into obscurity until nearly 20 years after his death. By that time, Archer J. P. Martin and Richard L. M. Synge were exploring an alternative to counterflow extraction to separate acetylated amino acids in the wool industry. Eventually they devised the idea of partitioning one phase while holding the other one stationary, and the result was the invention of liquid−liquid partition chromatography in 1941 (*42*). This led to their receiving the 1952 Nobel Prize in Chemistry for their invention of partition chromatography.

In his Nobel lecture, Martin casually revealed that he, in collaboration with A. T. James, had devised a mechanism for gas−liquid chromatography using a liquid stationary phase coated onto a solid packing, in combination with a gas mobile phase. A landmark publication followed shortly thereafter in 1952 describing the invention of modern gas−liquid chromatography (GC) and its application to the separation and quantitation of C_1−C_{12} volatile fatty acids (*43*). The first commercial GC instrument manufactured was the Perkin-Elmer model 154 Vapor Fractometer in 1955. Early GC column packings included ground firebrick, laundry detergent, and whatever else food chemists could experiment with and were used in combination with early thermal conductivity detectors.

GC expanded rapidly over the three decades since its invention in 1952. Major milestones in GC development came with column phase technology, flame ionization and electron capture detectors, cold on-column sample inlet systems, and headspace concentrators (*44*). The introduction of robust, efficient, and reproducible fused-silica capillary columns in the late 1970s by Hewlett-Packard and J&W Scientific propelled GC as a ubiquitous tool in food analysis laboratories (*45*). An advantage of capillary columns over packed columns is their greatly increased separation efficiency, lower temperature, chemical inertness, and

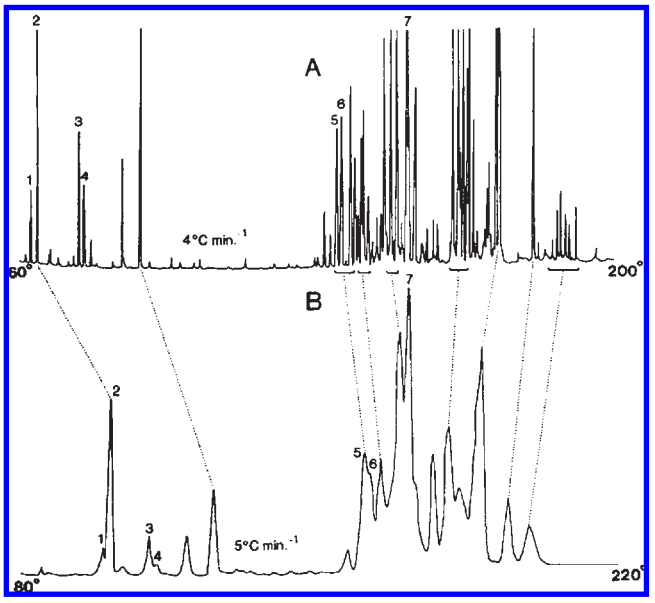

Figure 3. Comparison of capillary column (**A**) versus packed column (**B**) GC separation of calmus oil. Reprinted with permission from ref *44*. Copyright 2002 Elsevier.

resistance to column bleed. Many trends in current progress can be seen to originate in the first two decades of the history of GC, but the invention of fused-silica capillary columns greatly increased the application of high-resolution GC for flavor and fatty acid analysis. **Figure 3** shows a typical comparison of the significantly enhanced resolution power of capillary column GC over packed column GC, using the same stationary phase for distilled calmus oil, which has a "spicy-aromatic" fragrance character (*44*). By the end of the century, GC had become the single most widely used analytical tool in chemistry, despite the restriction that analytes needed to be volatile.

A significant milestone in liquid chromatography was the development of high-performance liquid chromatography (HPLC) by James Waters (*46*). Commercial instruments introduced in 1967 by Waters Corp. made HPLC a valuable, widely used tool for food chemists and led the way toward solving difficult separation problems by providing enhanced speed, sensitivity, and resolution. In 1972 Waters introduced the model 6000 with the first dual-reciprocating piston pump (6000 psi), an innovation in precision solvent delivery that delivered nearly pulseless column flow to increase the signal-to-noise ratio at the detector. Subsequently, HPLC evolved into an important food analysis tool for separation of mixtures of compounds and their quantitation, initially using refractive index and ultraviolet detectors. The 1978 introduction of the first commercial, disposable miniature silica-based solid phase extraction (Sep-Pak) cartridges by Waters became the predominant technique for food sample enrichment and purification by removing interfering substances prior to HPLC analysis.

Other new chromatographic and electrophoretic techniques were introduced for application to food analysis, including thin-layer chromatography (1938), paper chromatography (1944), and more recently sodium dodecyl sulfate−polyacrylamide gel electrophoresis (SDS-PAGE, 1967), two-dimensional PAGE (1975), ion chromatography (1975), capillary electrophoresis (1989), and supercritical fluid chromatography (1995).

GC and HPLC have the broadest applications to food analysis. Current analyses of sugars, polysaccharides, amino acids, proteins, vitamin, colors, herbicide and antibiotic residues, and other food constituents would not be as be as rapid, productive, or information-rich without the application of HPLC. New phases continue to be developed that offer expanded resolution or speed of analysis. Similarly, fatty acids, lipid components, flavors, pesticide residues, steroids (cholesterol), and other food components are routinely analyzed by capillary GC. Prior to the development of chromatography, food chemical analysis required repetitive crystallizations, fractional distillation, or chemical derivatization techniques.

DAWN OF THE MASSIVE INSTRUMENTS (1940−1980)

The history of mass spectrometry dates back more than 100 years and has its roots in physical and chemical studies regarding the nature of stable elemental isotopes. Mass spectrometry is an analytical technique that identifies chemical composition based on the mass-to-charge ratio of charged particles as they undergo chemical fragmentation and pass through electric and magnetic fields. J. J. Thomson was the first to measure the m/z values of positive ions, and he can rightfully be called the father of mass spectrometry. In 1919, Francis Aston constructed the first velocity focusing mass spectrograph with a mass resolving power of 130, for which he won the Nobel Prize in 1922 for mass spectrometry. Aston's design improvements of the early mass spectrometer (MS) continued through the 1930s, with resolving power increasing to 2000. The first commercial mass spectrometer was the model 21-101 constructed in 1942 by the Consolidated Engineering Co. These early instruments were generally large, expensive, difficult to work with, and more suited to solving research problems. They were do-it-yourself, room-sized instruments that had to be used with vacuum pumps and pneumatic devices and were driven by large racks of analogue electronics (*47*).

In 1963, Associated Electrical Industries (now Kratos Analytical) introduced the MS-9 as the first high-resolution mass spectrometer sold in the United States, which was applied by the flavor and fragrance industry for accurate mass determinations. The concept was that a high-resolution mass spectrometer could measure mass with sufficient accuracy to deduce the elemental composition of organic compounds (*48*). These MS instruments, nicknamed "workhorses", led to significant advances in the knowledge of flavors and identification of food components.

A breakthrough development occurred in 1960 with the interfacing of a mass spectrometer as the detector for gas chromatography by Roland Gohlke and Fred McLafferty (*49*, *50*). Through this powerful combination, GC provided the separation of volatile compounds and MS yielded unambiguous chemical identifications. Subsequently, major advances in flavor chemistry and flavor analysis were enabled by the GC-MS identification of trace-level volatile components as commercial instruments were made available in the late 1960s (**Figure 4**).

One of the major developments that led to wider distribution and adoption of GC-MS instruments in food analysis laboratories was the development of commercial quadrupole MS technology by Finnigan Instruments that replaced large, expensive, capricious magnetic sector instruments (*51*). Hewlett-Packard licensed the technology, which eventually led to the development of their computerized 5970 Mass-Selective Detectors for GC—reliable and relatively simple instruments that could be routinely used by food chemists. GC-MS expanded rapidly over the remaining half of the 20th century after the introduction of relatively low-cost but reliable benchtop instruments in the 1980s. Progress in food chemistry continues to be rapid in comprehensive two-dimensional 2D-GC, fast analysis, detection by atomic emission, and time-of-flight mass spectrometry and with applications to process analysis.

Early MS instruments in the 1960s had oscillographic trace outputs that spewed-out bar graphs of mass spectra on a 3 ft

Figure 4. Early Hitachi RMU-6E GC-MS instrument employed to identify volatile compounds in flavors (1969) (courtesy International Flavors & Fragrances).

Figure 5. Author using a Hewlett-Packard 5985 GC-MS instrument for identification of dairy flavor volatiles (1982) (courtesy Kraft Foods).

length of photosensitive paper with the push of a button! These were gradually obsolesced in the 1980s by computerized graphic displays of MS spectra, and the ability to match unknown compounds with MS library databases (**Figure 5**).

Nuclear magnetic resonance spectroscopy (NMR) was being developed initially as a tool for analysis of pure organic compounds in the late 1940s. NMR spectroscopy of a bulk material was first demonstrated independently by Felix Bloch and Edward M. Purcell in 1945. NMR is the most powerful analytical technique, because it provides unambiguous structure identification of organic molecules. Whereas NMR is not nearly as sensitive an analytical technique as MS, it requires minimal sample preparation, provides rapid analysis, and offers the potential to run multiple tests on a single sample. The early commercial NMR instruments of the 1960s were 60 and 100 MHz proton and ^{13}C instruments manufactured by Varian Associates, which were applied to aroma compound identifications by the flavor industry (**Figure 6**). Later in the 20th century, high-resolution spectrometers were constructed with 300−800 MHz fields that were coupled to computers with Fourier transform pulse sequences. In food applications, NMR can be used to measure moisture content, and it can be applied to food lipids to measure the degree of conjugated double bonds in fatty acid mixtures in an easy and nondestructive manner.

Figure 6. Varian HA-100 (100 MHz) NMR applied for identification of flavor compounds (1968) (courtesy International Flavors & Fragrances).

By the late 1980s, all-digital instruments incorporated improvements developed in both commercial and academic laboratories that allowed them to be more affordable and much smaller, occupying several linear feet on a laboratory bench rather than considerable floor space. During this period, newly designed instruments provided the ability to measure food components that were different from or beyond what was previously possible. These new tools were a source of major innovations in food technology and were able to elucidate many issues about the nature of modern chemistry of foods, such as the correct assignment of sensory attributes to specific flavor molecutles.

KEY ENABLING TECHNOLOGIES

Three significant converging technological advances occurred during this period which contributed to significant advances in food analysis capabilities.

Semiconductor Technology. Intel Inc. introduced its first 8-bit microprocessor, the 4004 chip, in 1971. The 4004 was capable of addressing up to 1 kB of program memory and up to 4 kB of data memory. In 1979, Intel developed a new 16-bit microprocessor, the 8088, and IBM engineers used it for the first personal computer. The combination of the new 16-bit microprocessor and the name IBM shifted the personal computer to a mainstream business tool.

Computing Technology. In 1981, IBM Corp. introduced the personal computer (PC), viewed as the most ubiquitous laboratory-enabling technology. The affordable and miniaturized PC became an integral component for data processing and graphics display as part of laboratory instruments such as IR and UV spectrophotometers, chromatography data systems, and mass spectrometers.

The impact of modern electronics is global in scope, especially during the past 50 years since semiconductor technology emerged and began to transform the world. Thirty-five years earlier, John Mauchly and J. Presper Eckert developed the ENIAC I (electrical numerical integrator and calculator). Through research sponsored by the U.S. military, the new computer used vacuum tubes, instead of switches and relays, to speed calculations. The only drawback was that it required 17468 vacuum tubes, which emitted considerable heat and needed frequent replacement. It covered 1800 square feet (167 m^2) of floor space, weighed 30 tons, and consumed 160 kW of electrical power (*52*).

Laser Technology. When the first working laser was reported in 1960, it was described as "a solution looking for a problem". Theodore Maiman created the first operating laser in May 1960 at the Hughes Research Laboratory in California, by shining a high-power flash lamp on a ruby rod with silver-coated surfaces (*53*). Twenty-five years later, the laser's distinctive qualities—its ability to generate an intense, very narrow beam of light of a single wavelength—were being harnessed by analytical chemistry for detection systems in spectrometers and chromatographic instruments. Computer optical disk drives for mainframe and personal computers were also developed that incorporated laser compact disks for storage and retreival of large mass spectrometry and chromatography data files.

The parallel developments of the laser, microprocessor, and personal computer industries and the convergence of these technologies with food chemistry provided phenomenal advantages for further miniaturization of food analysis, accuracy, speed, and limits of detection.

MODERN AGE OF FOOD ANALYSIS

Food analysis is often the beneficiary of technical advancements (chromatography, separations, MS, FTIR, and NMR spectroscopy) that were initially developed for the petroleum, pharmaceutical, chemical manufacturing, environmental, and natural products chemistry areas. Beginning with the commercialization of the Beckman Acidimeter in 1934 through the Caliper LabChip microchip for fluid handling in 1996, the Chemical Heritage Foundation has identified "50 chemical laboratory instruments that changed the world in the 20th century" (*54*). These key instruments were recognized as having a significant impact across a broad spectrum of chemical research and analysis. Through technology adaptation, many of these key instrumental capabilities were applied by food chemists to develop new analytical methods and procedures for measuring food components. For example, the pharmaceutical industry drove the need for chiral separations of asymmetric organic compounds. Whereas one enantiomeric isomer may exhibit the desired pharmacological activity, the opposite enantiomer could potentially cause undesired side effects (e.g., (*S*)-thalidomide). Chiral chromatography was readily adapted for authentication of natural flavors to determine the most sensory-active enantiomers during discovery of new flavor compounds. Capillary electrophoresis,

which was initially introduced by Beckman in 1989 for biochemical separations, was readily applied to the analysis of pea oligosaccharides, citrus pectins, casein aand whey proteins, gliadins and glutenins in wheat, and myoglobin proteins and peptides in foods (*55*).

Multidimensional or hyphenated instruments employ two or more techniques either sequentially (such as GC-MS and GC-MS/MS) or in parallel (GC-IR-MS). Fragment ions can only be used for structure determination, and a tandem instrument with two quadrupole mass analyzers allows an analyst to "piece together the structural puzzle" to deduce the origin of fragment ions. The high-performance liquid chromatography−tandem mass spectrometry (LC-MS/MS) technique has been useful for sequencing food peptides and proteins such as caseins.

Similarly, comprehensive two-dimensional GC×GC and LC×LC instruments became available within the past five years that are capable of significantly enhanced separation of complex mixtures (*56*−*58*). These instruments rely on combinations of different chemical selectivities to achieve separations of flavors or phenolic antioxidants in beverages. Time-of-flight (TOF) tandem mass spectrometers with matrix-assisted laser desoprtion ionization (MALDI) are now used routinely for rapid sequencing of amino acids in proteins.

Simultaneous with the progressive development of new instruments with increased analyte specificity over the past 60 years was the ongoing trend toward lowered limits of detection in food analysis. Relative sensitivities of analytical tests for minerals and elements over the early period have been tabulated (*6*). New and improved detectors for GC (flame ionization, electron capture, chemiluminescence, pulsed flame photometric, MS) and HPLC (refractive index, ultraviolet, fluorescent, diode array, evaporative light-scattering, MS) provided micromole to picomole enhancements in sensitivity depending on the analyte/application. Spectroscopy and spectrometry instruments (MS, IR, UV, NMR, atomic emission) afforded a reduction in detection limits from nanomole to picomole. As analytical instruments became increasingly sensitive, additional components in foods that were previously undetectable could be quantified. Furthermore, carcinogenic compounds that formerly had been below detection limits could now be measured. This had significant implications in the area of food law and food regulation. Perhaps the best-known example is the 1958 amendment to the U.S. FD&C Act of 1938, known as the "Delaney clause", named after the Congressman who chaired the Congressional subcommittee (*59*). The Delaney clause prohibits the use of food additives that have been shown to cause cancer in humans or animals, without consideration of the concentration level at which a toxic effect is induced. Virtually all foods contain traces of carcinogenic substances from environmental and natural sources (e.g., safrole in sassafras and cinnamon), and this law had broad ramifications (*59*). It required processed foods to be reformulated to eliminate any additives (e.g., those containing trace impurities) that now had measurable amounts of carcinogens, even though they probably did not consitute a health risk. The Delaney clause was first invoked in 1959 when traces of the cancer-causing herbicide aminotriazole were discovered on cranberry plants from Oregon and Washington, causing sales of cranberries to plummet during the week of Thanksgiving. Pesticide use was removed from the Delaney clause in 1996 by an amendment to the U.S. Food Quality and Protection Act (*60*).

Specific measurements of food quality include food safety (microbiological) testing, nutrient content, pesticide residue testing, and biotechnology applications (use of genetically modified organisms, GMOs). The latter three areas typically involve development and application of new chemical analyses. The requirement for nutrition labeling of foods juxtaposed with parallel advances in the fields of moleular biology, biochemistry, and genetics has spawned the development of new chemical methods to measure carbohydrates, fat, essential fatty acids, protein, fiber, macrominerals (Ca, Mg, K, Na, P), trace minerals (Co, Cu, Fe, Cr, Mn, Se, Zn), and vitamins in a variety of food and beverage matrices.

Sampling. Perhaps one of the most critical aspects of the analytical process is obtaining a representative food sample for analysis. Consideration for how to conduct appropriate sampling can occur on two levels: (1) developing a protocol for sample collection (e.g., field crop location, manufacturing, marketplace, or home), assessing the statistical number of samples required, and determining whether the food should be sampled in raw, cooked, or processed form; (2) compositing the sample and selecting a representative aliquot from a homogenized multicomponent food prior to analysis. A homogeneous sample is necessary prior to the performance of chemical analysis to ensure that the result represents the composition of the overall food sample (e.g., a pizza that contains bread crust, cheese, tomato, mushroom, sausage, and green pepper components). Care must be taken to avoid contaminating the sample or exposing it to excessive heat, which can cause loss of volatile flavor components or accelerate decomposition of labile food components. The food chemist may need to consider the chemical stability of the targeted analyte to appropriately blend a food under frozen, inert atmosphere, or low-light conditions (e.g., for vitamin analyses).

Sample Preparation. Challenges remain for the analysis of individual chemical species in food systems because of their complex multicomponent structure. Despite the availability of modern techniques of separation and identification, such as GC-MS and LC-MS/MS, rarely is it possible to load a syringe with a food sample and directly inject it into an analytical instrument to obtain a sensible result! Sample preparation and extraction remain among the most time-consuming and error-prone steps in the food analysis process (*61*). However, they are critical procedures because food scientists need to isolate and concentrate a wide range of analytes from complex and varied food matrices. Sample preparation typically involves pH adjustment, extraction with organic solvents, solid phase extraction, cleanup (filtration, liquid−liquid partitioning), and concentration for subsequent analysis via chromatography or other methods.

Recently developed automated sample preparation techniques that can be easily integrated with other analytical systems offer productivity improvements for many food analysis laboratories. Automated preparation techniques incorporate either low-volume solvent extraction or solvent-free thermal desorption, and in most cases they can increase the efficiency relative to conventional solvent extraction. For example, the Mojonnier ether extraction method (AOAC 922.06) typically requires 2−3 h and 110 mL of solvent for determining the fat content in chocolate, whereas pressurized fluid extraction (accelerated solvent extraction (ASE), Dionex) reduces the extraction time to 18 min and solvent use to less than 20 mL (*62*). Other examples include supercritical fluid extraction, thermal desorption, solid phase extraction, solid phase microextraction (SPME), and stir-bar sorptive extraction (SBSE). Modular systems are now readily available that automate these procedures and interface them to analytical instruments, such as GC, GC-MS or HPLC.

Macrocomponent Analyses. Proximate analyses (crude fat, protein, moisture, soluble solids, ash) have been typically conducted by classical wet chemistry methods that were tailored for analyses of food products (**Table 2**) (*12*). New developments and improvements in instrumental techniques are providing rapid,

Table 2. Comparison of Representative Food Analysis Methods[a]

analyte	classical "wet" method	instrumental method
moisture	Karl Fischer dry fruits/vegetables **967.19 E-G** cocoa **977.10** vacuum oven meat/poultry **950.46**	near-infrared dry fruits/vegetables **967.19 B-D** microwave oven meat/poultry **985.14**
sugars	total dextrins **988.12** Munson−Walker **906.03** sucrose (cocoa) **920.82**	HPLC milk chocolate **980.13** ion chromatography
total dietary fiber		enzymatic−gravimetric **985.29**
protein	Kjeldahl **955.04; 988.05** milk **991.23**	Dumas combustion/GC meat **992.15** capillary electrophoresis
fat	*total* (*crude*)*:* Mojonnier ether extraction flour **922.06** milk **989.05** Soxhlet ether extraction meat **960.39** Roese−Gottlieb (milk) **905.02**	*total* (*crude*)*:* microwave-solvent extraction meat **985.15** accelerated solvent extraction *fat as fatty acid glycerides:* gas chromatography fish oil fatty acids **991.39**
cholesterol	titrimetric **941.09**	gas chromatography **994.10**
vitamin A	Carr−Price **974.29**	HPLC **2001.13; 2002.06** (milk)
minerals (Ca, Cu, Fe, Mn, Zn)	atomic absorption spectrometry **991.25; 999.10**	ICP−atomic emission spectrometry
metals (Pb, Cd, Hg)	mercury **971.21**	ICP−mass spectrometry

[a] AOAC Official Analytical Method indicated in **bold**.

automated alternatives to the classical food analysis methods. Current regulatory requirements for food manufacture obligate not just the analysis of total fat content (e.g., Mojonnier) but also the characteristics of the fat, that is, saturated, monounsaturated, polyunsaturated, monoglycerides, diglycerides, cholesterol, etc. Classical total protein determinations were historically based on nitrogen content (the Kjeldahl technique); however, modern electrophoretic and chromatographic methods were developed that enable rapid and specific amino acid and peptide assays. Total carbohydrate values are required to be listed as specific components: sugars, sugar alcohols, dietary fiber, soluble fiber, and insoluble fiber. Moisture content has been redefined to specify the states of water as being "free", "bound" (e.g., hydrogen bonding to sugars, salts, proteins), or "adsorbed" (e.g., with phospholipid layers, starch), and each of these modes requires a specific analytical measurement.

HPLC is a very powerful and versatile technique for analyzing and purifying biomolecules and, consequently, is a well-established mode for food and beverage analysis. Ongoing advances in column supports, bonding chemistry, porous particles, and packing materials have enabled increased speeds and efficient separations of a wide range of organic and inorganic food analytes from low parts per million to high parts per billion levels. Related column techniques that involve separation by either ionic mobile phases or charged fields are ion chromatography and capillary electrophoresis, respectively. Typical food analytes quantified by these techniques include mono- and disaccharides, aspartame, phospholipids, vitamins, caffeine, organic acids, ionic species, peptides, and proteins. Highly sensitive fluorescence detectors for HPLC instruments enable lower limits of detection for vitamins, proteins, aspartame, and mycotoxins.

Spectroscopic techniques are highly desirable for analysis of food macrocomponents because they often require minimal sample preparation, provide rapid analysis, and have the potential to run multiple tests on a single sample. These advantages particularly apply to nuclear magnetic resonance (NMR), infrared (IR), and near-infrared (NIR) spectroscopy. The latter technique is routinely used as a quality assurance tool to determine compositional and functional analysis of food ingredients, process intermediates, and finished products.

Microcomponent Analyses. Volatile compounds are most often analyzed in foods, flavors, and aroma systems. Since the 1960s, the combination of gas chromatography and mass spectrometry has become an essential tool to identify flavors (*63*, *64*). More recent developments in capillary column technology and the use of various headspace concentrators (equilibrium, dynamic/Tenax, vacuum, solvent-assisted flavor evaporation, solid phase microextraction, stir-bar sorptive extraction) have shortened the assay time and increased limits of detection for potent flavor components (*65*). GC−olfactometry as a sensory-directed technique has significantly advanced the field of flavor chemistry during the analysis of complex flavor mixtures (*66*). It enables the relative contributions of individual flavor components to be assessed in real time as they are being separated while allowing the food chemist to assign aroma descriptors ("fruity", "green", "roasted") to chromatographic peaks that have sensory impact.

Additional trace analytes in foods include colorants, pigments, vitamins, and minerals. Research on bioactive "functional" food compounds relies on the development of new assays with increased sensitivity and specificity to measure efficacious phytochemical components (anthocyanins, polyphenolic compounds), which are frequently colored. Atomic spectrometry methods including atomic absorption, atomic emission, and elemental mass spectrometry are routinely used to measure minerals (e.g., calcium, zinc) and heavy metals (e.g., lead, cadmium, mercury) in food products (*67*). Inductively coupled plasma atomic emission spectrometry (ICP-AES) and inductively coupled plasma mass spectrometry (ICP-MS) offer the advantage of providing simultaneous multielement measurement in food samples. In these techniques, samples are vaporized, atomized, and excited in a high-temperature argon plasma. Detection limits are 1−100 ppb for ICP-AES and 1−100 ppt for ICP-MS. Microelemental analysis by ICP-AES has been used to differentiate country of origin and geographic growing conditions for potatoes, coffee, pistachios, and fresh strawberry, blueberry, and pear (*68*), by simultaneously measuring relative differences in elemental concentrations. Recently developed micro X-ray fluorescence spectrometry instruments provide a nondestructive technique for food quality control applications to rapidly analyze metallic elements, minerals, and heavy metals at parts per million sensitivity limits. Analytical measurement of toxicological residues in foods including pesticides, aflatoxins, and other mycotoxins have been devised by the development of chromatographic, spectrographic, and immunochemical methods for assaying these compound classes.

Enzymes, microbes, and antibodies have been exploited as biosensors to rapidly measure the presence of amylases or proteases in foods, which can cause starch thinning or bitter flavors, respectively. Enzyme-linked assays have been used to measure vitamins, antibiotic residues, microbial toxins, various sugars, ethanol, and carbon dioxide (*69*). In certain cases, enzyme

activity assays are practical food safety probes to measure whether adequate processing of a food product has been achieved.

Electrophoretic methods have been applied to food analysis, initially using SDS-PAGE for separation of milk proteins (caseins, whey) and cereal proteins (glutenin, gliadin, zein) (*55*, *70*). Variations include isoelectric focusing, 2-D gel elctrophoresis, and isotachophoresis. Analyte separations are a function of their mass-to-charge ratios in an externally applied electric field. Gel electrophoresis was demonstrated to be especially useful in protein fingerprinting for the authentication of specific animal species to detect labeling fraud. Applications include the identification of specific proteins in red snapper, buttermilk powder, egg pasta, citrus isozymes, and cow's milk in goat cheese (*55*, *70*, *71*). Following its commercial introduction, capillary electrophoresis (CE) was readily substituted for SDS-PAGE in the 1990s to develop new methods for food protein analysis (*55*, *72*−*75*). CE provides analytical separation and reproducibility that are superior to those of gel electrophoresis and are comparable to those of HPLC, with a range of detector options including UV, diode array, fluorescence, conductivity, and MS (*76*). CE applications include protein authentication to identify specialty cheeses produced with vegetable coagulant instead of rennet (*77*), monitoring specific flavonoids and amino acids in orange juice for freshness (*78*), determining D-isocitric acid as a marker for authenticity of orange juice (*79*), and measuring phenolic acids in extra virgin olive oil (*80*).

Combinations of chromatographic, NMR, isotopic, and enzyme-linked methods have been developed to screen and detemine the authenticity of suspect food products and ingredients, as prompted by economic fraud (*19*−*23*). Ironically, adulteration occasionally persists 100 years after creation of the Food and Drug Act in Dr. Wiley's era. Modern examples include partial substitution of corn syrup for honey; organic acids and sugars for apple juice; and benzaldehyde for almond extract.

FUTURE DEVELOPMENTS AND HORIZONS

Looking toward the next century, any prediction about new developments in food analysis must consider the convergence of multiple influences. A first consideration involves the natural evolution of scientific discoveries, which proceed at their own pace, but are accelerating due to rapid sharing of information via the Internet and electronic media. New technological advances will emerge, driven by old-fashioned Edisonian experimentation and innovation. The current desire for smaller analytical instruments, increased speed of results, lowered detection limits, easier operation, and portable applications of analytical measurements in food production or field crop environments other than in the traditional laboratory will continue.

The food analytical laboratory of the future will likely have glassware and equipment that resemble those of current laboratories; however, the progression to smaller instruments, computers, and data collection devices is imminent (*81*). Laptop computers now reside in most laboratories, but miniaturization of electronic hardware and more powerful software systems will likely drive integrated instrument control and data collection systems that incorporate electronic notebooks. Bar-coding systems will evolve to track and monitor large numbers of samples. Radio frequency identification (RFID) systems are starting to be used in the commercial and industrial sectors that have yet to be integrated into laboratory environments. Automation of instruments and analytical measurements is a likely expectation for the future of routine food assays. Smaller instruments will integrate microfluidic designs that use smaller sample volumes and fewer solvents and require less cleanup and waste disposal. Flexible laboratory designs, moveable casework, and overhead utility hook-ups (gases, water, electricity, vacuum) will provide the ability to quickly change from one analysis project to another as new applications dictate.

The needs of food-processing and agricultural production will continue to create demand for improved analytical methods that can measure new attributes, features, or molecular components in food products or ingredients while providing more analyte information at lower detection limits. Instrumental improvements in mass spectrometers enabled state-of-the-art limits of detection that evolved over the 1970−2000 period from picomole (10^{-12}) to femtomole (10^{-15}). The progression over the next couple of decades is toward attomole (10^{-18}) limits for the ability to detect thousands of individual molecules. Ion detectors for mass spectrometry applications are currently being developed at the frontiers of analytical capability using electrode arrays (*82*). The convergence of biomedical advances, health and nutrition needs, and food choices will likely evolve into the need for information-rich, real-time analytical measurements that address bioavailability and delivery. As the competitive marketplace evolves, new regulatory requirements for food analysis will surface, driven by governmental and political forces.

Continued research in the areas of health-promoting constituents of foods (e.g., carotenoid phytochemicals and polyphenolic antioxidants) will spawn the development of new assays to measure their presence in foods and changes occurring during processing. Flavonoids, isoflavones, isothiocyanates, organosulfur compounds, carotenoids (lycopene, lutein), saponins, and capsaicinoids are active areas of research related to potential benefits for cancer prevention, antiinflammation, antioxidant effects, and assistance to the immune system (*83*, *84*).

Rapid methods for testing raw ingredients, product quality, and process monitoring will undoubtedly experience continued growth. The percentage of rapid tests should increase dramatically in the coming years, as diagnostic assay companies provide performance improvements. Food-processing companies will readily adopt rapid analytical methods to screen raw materials to diminish the risk of food safety incidents and ensure compliance with regulatory standards. Near-infrared (NIR) and mid-infrared (MIR) spectroscopy applications are currently being examined for online quality monitoring in food processing plants (*85*). ATP bioluminescence assays using the firefly enzyme luciferase are commercially available as test kits to monitor food residues and microorganisms during the sanitation of food processing equipment (*86*). Fiber optic biosensors using different surface chemistries and antibody complexes are being explored for the detection of foodborne pathogens (*Escherichia coli*, *Listeria*, *Salmonella*) (*87*). Nanoparticle sensors are under development as DNA probes for the detection of microbial pathogens in foods using semiconductor, metallic, metal oxide, or polymeric materials (*88*). Aroma sensor arrays are being designed using chemically responsive dyes that provide unique colorimetric patterns for individual odorants (*89*). Future technology refinements of electronic noses (*90*, *91*) and electronic tongues (*92*) will likely find process monitoring applications for flavor quality.

Trends are emerging through the miniaturization and portability of analytical instruments. Cutting-edge chromatography technologies utilize credit-card-sized polyimide-based fluidic chips in nanoflow channel HPLC-MS instruments to quantitate peptides (*93*). Field-portable instruments are continuing to be developed, which could be applied to monitor crop ripening and assess fruit and vegetable quality.

Pesticide residue testing of foods is routinely performed to comply with various international food regulations that vary by country. Pesticide testing relies on analytical methods as screening tools to measure whether an approved pesticide is being correctly applied for specific food crops. As future pesticides are developed and approved for food use, new analytical methods (usually GC or HPLC) will need to be subsequently developed to quantify their presence and levels in foods.

The engineering of new genetically modified food crops has and will continue to provide impetus for advancement of new analytical methods to screen for compositional or antinutritive differences compared with conventional food crops. HPLC-MS methods have been developed for sequencing food proteins in genetically modified crops to characterize peptide fragments and other molecular features that correspond with those of known food allergens (*94*).

The high-throughput testing demands of the food industry will likely create financial incentives for new generations of analytical instruments that can make specialized measurements. As the need for global food supply traceability grows, increasing numbers of food products and ingredients will need to be routinely tested. Requirements for new analytical laboratory instruments will emphasize performance, sensitivity, reliability, simplified use, and low-cost for high-volume, routine assays. The transformative dynamics of the revolutionary years from 1930 to 1950 are still at work at the beginning of the 21st century. No doubt, analytical instruments have and will continue to profoundly shape the future of food chemistry and the food industry.

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