CHEM 4590
Radiochemical methods: basics
Neutron activation analysis (NAA):  
Activity is induced in samples by neutron irradiation. 
Resulting radioactivity (gamma rays) is measured. 
About 70 elements can be determined.

Tracer methods:  
Radioactivity is induced by a measured amount of a radioactive species. 
e.g. nuclear medicine (PET scan).

Isotope dilution (ID):  
A known quantity of radioactively-labelled analyte is added to the sample. 
The analyte is pulled down or purified, and its radioactivity is measured. 
About 30 elements + biochemical compounds.

As Jen has already given us a very informative presentation on trace imaging, this lecture will cover only NAA and ID. ID was already partly covered by Bofan in his seminar, but I will give more details here.
Neutron activation analysis (NAA)

- A method of trace elemental analysis
- NAA method first developed by George de Hevesy and Hilde Levi in 1936*
- Really emerged in the late 1940’s and in the 1950’s
- Radioactivity is induced in samples by neutron capture
- The gamma radiation emitted during nuclear decay is measured at wavelengths unique to each element.

Main Purpose of NAA:

Targets an element for quantitative analysis by transforming it into an unstable nucleus which emits gamma radiation.

\[
\frac{A}{Z}X + ^0_1n \rightarrow \frac{A+1}{Z}X
\]

Where X = element symbol, e.g. Co
n = neutron symbol
Z = atomic number or number or protons (+ve charges) in the nucleus
A = atomic mass = total number of proton and neutrons

\[
\frac{59}{27}Co + ^0_1n \rightarrow \frac{60}{27}Co
\]

The gamma emitting process occurs in 2 steps as seen on the next slide.
Prompt gamma radiation is not used for analysis. It is too intense, would saturated detectors and be harmful to exposed workers.
To get back to the specific example of cobalt:

Note how the subscript and superscript numbers are additive. A beta particle has no mass relative to neutrons and protons. It has a charge of $-1$ which will change the nature of the nucleus when a beta particle is emitted.
If a positron is emitted, the reaction would be:
Main steps in NAA:

Sample is irradiated with neutrons

Exposure time usually 3 to 5 times isotope half life

\[ ^{59}_{27}Co + ^1_0n \rightarrow ^{60}_{27}Co \]

Produces a radioactive isotope: atomic number does not change.

In the example above Co remains Co but a neutron has been added to its nucleus, making it unstable thus radioactive.

The sample is allowed to cool to eliminate short lived interferences

New isotope emits gamma radiation when decaying

Measured at specific \( \lambda \) to determine the element’s concentration or amount.
**γ-Ray emission:**

Some α and β emission processes, as well as neutron capture, lead to excited nuclei. These nuclei return to the ground state by releasing quantized γ-rays.

γ-Rays often have the same energies as X-rays, but are from a different source.

**γ -Rays: nuclear relaxations.**

**X-Rays: electronic relaxations (when pulling out inner shell electrons like in X-ray electrospectroscopy).**

γ -Ray emission spectrum: characteristic to each nucleus and useful for identification.
Radioactive decay rates

Each radioactive element or radionuclide has its own half life and decay rate.

Half life is how long it takes for a radionuclide population \( N_0 \) to decay to 50%.

Rates must be looked at statistically as each nucleus originated at a different time, and behaves slightly differently.

For a large distribution of nuclei of a single type:

\[
- \frac{dN}{dt} = \lambda N
\]

\( N \) = number of radioactive nuclei of one kind
\( \lambda \) = decay constant
Integrating over the interval $t = 0$ and $t = t$ ($N_0$ to $N$):

$$\ln \frac{N}{N_0} = -\lambda t$$

or...

$$N = N_0 e^{-\lambda t}$$

$$\ln \frac{N}{N_0} = -\lambda t$$
Sources of neutrons:
- Reactors
- Radionuclides
- Accelerators

Thermal neutrons:
Have been slowed down to $< 0.1$ eV K.E. (from MeV) by a moderating material ($H_2O$, $D_2O$, paraffin).

Used analytically for most elements.

Fast neutrons:
14 MeV, used for lighter elements such as N, O, F, Si.
Sources of thermal neutrons

From nuclear reactors

Flux: $10^{11}-10^{14}$ neutrons cm$^{-2}$s$^{-1}$

Detection limits: $10^{-3}$ to $10^{1}$ µg

From radionuclides

Flux: $10^{5}-10^{10}$ neutrons cm$^{-2}$s$^{-1}$

Detection limits: not as good

Commonly used: $^{238}$Cf, $t_{1/2} = 2.6$ y.

Decay (3%) is by fission (3.8 n/fission).
Sources of fast neutrons

From accelerators (for lighter elements)

Ion source generates and delivers deuterium ions (D⁺) which are then accelerated to 150 keV to a target with adsorbed tritium:

\[
\begin{align*}
^{2}_1H + ^{3}_1H & \rightarrow ^{4}_2He + \ ^{1}_0n \\
\text{14 MeV}
\end{align*}
\]
How do neutrons interact with matter?

- They have no charge and can thus approach other particles without coulombic repelling forces.

- Most important reaction: neutron capture. Product has same Z, A+1, and is highly energetic from binding with the neutron (ca. 8 MeV).

- Result: prompt gamma-ray emission (among others).

e.g.

\[ ^{23}_{11}\text{Na} + ^{0}_{1}n \rightarrow ^{24}_{11}\text{Na} + \gamma \]
Irradiation: duration is generally $[3-5 \times t_{1/2}]$ of the analyte.

Counting: immediately after cooling.

Non destructive route means the sample is never taken out of the instrument after its irradiation. The cooling period is for prompt radiation to take place. $R_x$ and $R_s$ are the radiation counts or intensity for the unknown and the standard. The standard and sample must be the same element and radiate at the same wavelength.
Destructive route means once irradiated, the analyte and/or standard needs to be purified or chemically modified. This is used when several elements are present in the sample and some that give away very intense radiation may mask others. This is often the case with sodium, often in high concentrations and with a high decay rate. Sodium needs to be extracted from the irradiated sample before analysis of other wavelengths may proceed.
Applications

- Biology
- Geology
- Archeology
- Forensic sciences
- Quality control
Accumulation of silver nanoparticles in mice tissues studied by neutron activation analysis

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Goals

- Mice were fed a diet spiked with silver nanoparticles
  - About 100 μg per day
  - Samples were taken at 2 and 4 months after administration
- Brain tissue, liver tissue and blood were analyzed
- Standards and samples were irradiated for 24 - 48hr
- $^{110}_{47}\text{Ag}$ produced prompt radiation, then $^{110}_{48}\text{Cd}$ was measured at 657.8KeV, 763.9KeV and 937.5KeV
Results:

- Using the non destructive method, the authors found that silver ended up in all samples: brain, blood, liver.
- They found high concentrations in liver tissue in 2 month samples, and after 4 months the Ag nanoparticles had partitioned into the brain and blood.
- Their conclusion was that Ag first affect the liver, then it stays in the body and affects other systems.
- See table of results next page.
### Table 1  Silver content in mice blood

<table>
<thead>
<tr>
<th>Gender</th>
<th>Content, µg/g dry weight</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Control (2 months)</td>
<td>0.09–0.73</td>
<td>0.3 ± 0.2</td>
</tr>
<tr>
<td>2 months of administration</td>
<td>0.9–4.5</td>
<td>2.5 ± 1.2</td>
</tr>
<tr>
<td>Control (4 months)</td>
<td>0.05–1.5</td>
<td>0.6 ± 0.4</td>
</tr>
<tr>
<td>4 months of administration</td>
<td>0.9–2.7</td>
<td>1.7 ± 0.6</td>
</tr>
</tbody>
</table>

### Table 2  Silver content in mice liver

<table>
<thead>
<tr>
<th>Gender</th>
<th>Content, µg/g dry weight</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Control (2 months)</td>
<td>0.8–1.6</td>
<td>1.2 ± 0.6</td>
</tr>
<tr>
<td>2 months of administration</td>
<td>37–293</td>
<td>140 ± 90</td>
</tr>
<tr>
<td>Control (4 months)</td>
<td>0.3–0.5</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>4 months of administration</td>
<td>9.6–104</td>
<td>65 ± 40</td>
</tr>
</tbody>
</table>

### Table 3  Silver content in mice brain (including silver in blood vessels)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Content, µg/g dry weight</th>
<th>Total Ag content, ng</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Control (2 months)</td>
<td>0.6–0.9</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>2 months of administration</td>
<td>5.2–10.6</td>
<td>6.8 ± 1.8</td>
</tr>
<tr>
<td>Control (4 months)</td>
<td>2.4–2.5</td>
<td>2.4 ± 0.1</td>
</tr>
<tr>
<td>4 months of administration</td>
<td>8.9–18.7</td>
<td>12.9 ± 2.9</td>
</tr>
</tbody>
</table>

Selenium in bread and durum wheats grown under a soil-supplementation regime in actual field conditions, determined by cyclic and radiochemical neutron activation analysis

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Goals:

- 2 types of wheat (bread and durum) were analyzed for Se content
- Se is used to fortify plants for better flour yield
- Irradiated for 20 h
- Allowed to cool for a month
- Sample were then digested with nitric acid, reacted with perchloric acid and then ascorbic acid was added to precipitate the Se ascorbate salt.
- Analyzed radiation for 2hr
Results

- Durum wheats had better bio fortification from Se than bread wheats
- The plants that received Se supplementation had a higher Se content
- Here the destructive route was used, where samples had to be taken out for acid digestion and precipitation of Se with ascorbic acid. This way, no radiation was interfering with that of $^{81}$Br.
Here impurities = trace metals
Goals:

- Heroin was sampled from two regions A and B
- Samples neutron-irradiated for 16 h
- Cooled for 5 to 20 days
- Counted for short and long-lived nuclides
Results: Concentrations differed in both regions, but at least 15 metals were found (limited by study).

Fig. 1. Concentration ranges and median values of 15 trace elements of original heroin powder (56 samples from Region A and 6 from Region B)

Overall Advantages and Disadvantages

Advantages
- Very low LOD for trace elements
- Can analyse many elements at once
- Non-destructive if possible

Disadvantages
- Creates nuclear waste
- Requires a neutron source
- Potentially harmful to scientists
- Because of these inconveniences, NAA is being replaced by ICP-MS
There are currently eight research reactors in Canada: two at AECL's Chalk River Laboratories (?) and six at universities.

The Chalk River reactors are based on CANDU technology.

The university reactors include five 20 kWth SLOWPOKE-2 reactors (at the University of Alberta (Edmonton), Saskatchewan Research Council (Saskatoon), Royal Military College (Kingston), Dalhousie University (Halifax), and L'Ecole Polytechnique (Montreal)), and a 5 MWth MTR-type reactor at McMaster University.

A Canadian-supplied SLOWPOKE-2 is also operated at the Centre for Nuclear Sciences, Kingston, Jamaica, and two SLOWPOKE-2 units - the original prototype at the University of Toronto and one at MDS Nordon's facility in Kanata - have been shut down).
The SLOWPOKE-2 is a low-energy, pool-type research reactor designed by AECL*. It is licensed to run unattended for short periods of time (e.g. overnight). AECL also designed a scaled-up version (2-10 MWth) of SLOWPOKE for district heating.

*AECL doesn’t exist anymore
The main piece of equipment is the SLOWPOKE nuclear reactor.

This small pool-type reactor operated from 1976 to 1997 with the original fuel, 1 kg of 93% enriched uranium. In 1997, thanks to an NSERC Major Installation Grant, the reactor was refuelled with 5 kg of uranium enriched to 20% in U-235. At full power of 20 kW, the neutron flux in the five inner irradiation sites of the reactor is $10^{12}$ /cm$^2$/s. The power and the neutron flux are highly reproducible and the reactor can operate unattended for up to 24 hours. It is used mainly for neutron activation analysis and for the production of radioactive tracers. For irradiating materials, access to the neutrons is through pneumatic rabbit systems. One of the six rabbit systems is automated and can be programmed to send a set of samples directly from reactor to detector.

Instrumentation is also available for training nuclear engineering students in reactor kinetics.

The neutron activation analysis laboratory adjacent to the reactor has four state of the art gamma-ray spectrometers with high-resolution germanium semiconductor detectors and mechanical sample changers. Other alpha, beta and gamma detectors include liquid, plastic and NaI scintillators, proportional counters and ionization chambers.
Research Program
The Laboratory is used primarily for NAA, which is a type of non-destructive chemical analysis used for measuring the concentrations of chemical elements in solids et liquids. When a substance is irradiated with neutrons it becomes radioactive and after it is removed from the reactor, atoms of the different elements emit gamma-rays which are detected.

Geochemistry - for the determination of rare-earths and platinum group elements which yield information on the formation of rocks and mineral deposits.

Materials science - for verifying the composition of new materials.

Archaeology - the chemical composition of ancient metal, ceramic and lithic objects is used to determine their provenance.

Medicine - studies on the toxicity of trace metals.

Environment - studies of heavy metal pollution in air and water, emissions of metals from the combustion of petroleum products. The results of our major study on atmospheric emissions from automobiles were instrumental in convincing the government to approve a new gasoline additive, less polluting than previous additives, which will significantly improve the quality of the air in our cities.
Isotope dilution methods
Isotope dilution procedure:

**Goal**: to determine the concentration of an analyte in a sample in the presence of other components.

1) preparation of a known mass $M_1$ of pure radioactive standard and measurement of $R_1$.

2) Addition of unknown mass $M_2$ (mixed within other components in sample).

3) chemical extraction of the analyte (active and inactive together) and determination of radioactivity $R_2$ from $M_1$ of this mixture.

4) \[ \frac{R_2}{R_1} = \frac{M_1}{M_1 + M_2} \] after correction (see next slide)
A question that would arise is: Why not simply do this by mass and not bother to measure radioactivity?

The answer is, when extracting or purifying any element, there is sample loss, so a yield associated with the procedure.

Then if $M_1$ is my original mass of standard, after extraction it is not true to say that $(M_1+M_2)_{extracted} = (M_1+M_2)_{real}$.

In fact, $(M_1+M_2)_{extracted} < (M_1+M_2)_{real}$

The ratio $R_2/R_1 = (M_1+M_2)_{extracted} / (M_1+M_2)_{real}$ is the only way to obtain the extraction yield and correct the calculation.

See a concrete example on the next two slides.
Let's imagine a 100-ml blood sample containing an unknown amount \( T_2 \) of chromium (non-radioactive).

To this sample, a standard sample \( (T_1 = 2 \times 10^{-4} \text{ mg}) \) of radioactive \( ^{51} \text{Cr} \) is added. The standard was first measured for radiation, \( R_1 = 1000 \) arbitrary units (a.u.).

Then, a chemical procedure is used to extract all \( \text{Cr} \) from the blood sample, radioactive and non-radioactive.

Total extracted \( \text{Cr} \) is weighed \( (T_1 + T_2)_{\text{extracted}} = 9 \times 10^{-4} \text{ mg} \).

Radiation is measured for total \( \text{Cr} \) extracted \( R_2 = 900 \) a.u.
If the extraction yield had been 100%, \( R_2 = R_1 \)

as the standard is the only source of radiation.

But here the extraction yield is

\[
\frac{R_2}{R_1} = \frac{900}{1000} = 0.9 \text{ (90%)}
\]

This way we can correct our \((M_1 + M_2)_{\text{extr.}}\) value.

\[
(M_1 + M_2)_{\text{true}} = \frac{(M_1 + M_2)_{\text{extr.}}}{0.9} = \frac{9 \times 10^{-4} \text{ mg}}{0.9} = 0.001 \text{ mg}
\]

And we can calculate the true \(M_2\) unknown value:

\[
0.001 \text{ mg} = 2 \times 10^{-4} \text{ mg} + M_2
\]

\[
M_2 = 8 \times 10^{-4} \text{ mg} = \text{ amount of Cr present in the original 100 mL blood sample.}
\]

(see bottom of next slide or application)
Isotopic and Nuclear Analytical Techniques in Biological Systems: A Critical Study

PART X. ELEMENTAL ISOTOPE DILUTION ANALYSIS WITH RADIOACTIVE AND STABLE ISOTOPE

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National Institute of Standards and Technology, Technology Administration, Department of Commerce, Gaithersburg, MD 20899, USA

The principle limitation to IDA is the availability of a suitable spike or tracer. The half-life and type of radiation emitted by a radiotracer is very important, as is the purity. The half-life must be long enough so that sufficient activity is available during the analysis for good counting statistics. However, too long half-lives can be a problem because of low specific activities, and storage and disposal problems. The type of radiation is important primarily in relation to the ease of measurement. There are suitable ($t_{1/2} > 10$ min) radiotracers available for most elements in the periodic table. The exceptions are He, Li, B, N, O, and Ne. Separated stable isotopes are available for some 80% of the elements of the periodic table. In addition, some of the 19 mononuclidic elements have long-lived radioisotopes, e.g. $^{129}$I and $^{230}$Th, which are suitable for IDMS.

IDA is applied to problems broader than chemical analysis. One example is its use in the determination of blood volume. The radioisotope $^{51}$Cr has been used in clinical practice since 1950 for this application (ref. 25). The technique relies on the extraction of blood, labelling with $^{51}$Cr, and reinjection into the body. Since the labelled blood is chemically stable, a second sampling after dilution/equilibration will provide the blood volume information. Because of the increased restrictions on using radioisotopes with humans, and inappropriateness of using them with pregnant women and infants, applications of stable isotopes for this measurement have been developed. Zeisler and Young have published a method based on NAA, $^{50}$Cr stable isotope dilution, and measurement of $^{51}$Cr induced activity (ref. 26). Similarly, mass spectrometric measurements of the stable isotopes directly are also possible and our being pursued (ref. 27).
Methods and problems in quantitative radiochemistry
Determination of i) total blood volume of an individual and ii) Cr concentration in blood, using isotope dilution measurements.

- Cr is composed of four main isotopes: $^{50}\text{Cr}$ (4.3%), $^{52}\text{Cr}$ (83.8%), $^{53}\text{Cr}$ (9.5%), and $^{54}\text{Cr}$ (2.4%).

- Upon exposition to neutron activation, only $^{50}\text{Cr}$ forms a species with a long enough $t_{1/2}$ (for $^{51}\text{Cr}$, $t_{1/2} = 28$ days). In comparison, $^{55}\text{Cr}$ has $t_{1/2} = 3.5$ min.

- $^{51}\text{Cr}$ can be a radiomarker for blood volume determination.
Step 1: Draw a blood ($V_1$) from a patient (Sample 1).

Step 2: Add a known amount ($W_1$) of pure $^{51}$Cr tracer. The volume of the sample is still $V_1$.

Step 3: Determine the decay rate $R_1$ of $^{51}$Cr in Sample 1, as a solution of total volume $V_1$.

Step 4: Determine the body blood volume: Reinject Sample 1 containing $^{51}$Cr in the patient. Let equilibrate. Redraw a new sample of volume $V_1$. Measure for decay ($R_2$) and obtain the dilution factor, $R_1/R_2$, then total volume.
1. A 0.25 M solution of radioactive $^{41}\text{CaC}_2\text{O}_4$ (50 mL) obtained by NAA is measured for its gamma ray radiation intensity and the value obtained is 5823 units. This solution is poured into a large container of unknown volume and the well water is stirred mechanically. A 50-mL sample of the mixed water is then collected and measured for radiation at an intensity of 48 units.

a) Determine the volume of the container.
b) Would it matter if rate measurements were made a few minutes apart? Justify.

2. A 1-g sample of pure neutron activated $^{28}\text{Al}$ emits a beta radiation rate of 2500 decays/min.

What would be the radiation rate of $^{28}\text{Al}$ in 15 g of $\text{Al}_2(\text{SO}_4)_3$?

a) 5950/min    b) 3053/min    c) 6150/min    d) 2959/min
3. A sample containing 10 g of $^{53}\text{Mn}$ is irradiated with neutrons to form $^{54}\text{Mn}$, half-life 312 days.
   a) How many grams of $^{54}\text{Mn}$ are left in the sample after 90 days?
   b) $^{54}\text{Mn}$ is a beta emitter. What is the product of radioactive decay?

4. An unstable nucleus decays by beta emission, then two nuclei of the product are combined in a reactor to produce $^{24}\text{Mg}$ plus an alpha particle. Determine the nature of the original isotope.
   a) Be  b) Li  c) C  d) N  e) Al

ANSWERS WILL FOLLOW IN A SEPARATE DOCUMENT