Nuclear Medicine: Physics and Imaging Methods (SPECT and PET)

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Based on J. L. Prince and J. M. Links, Medical Imaging Signals and Systems, and lecture notes by Prince. Figures are from the textbook except otherwise noted.
Lecture Outline

• Nuclide Imaging Overview
• Physics of Radioactive Decay
• Single Photon Emission Computed Tomography (SPECT)
• Positron Emission Tomography (PET)
• Image Quality consideration
  – Resolution, noise, SNR, blurring
What is Nuclear Medicine

- Also known as nuclide imaging
- Introduce radioactive substance into body
- Allow for distribution and uptake/metabolism of compound ⇒ *Functional Imaging!*
- Detect regional variations of radioactivity as indication of presence or absence of specific physiologic function
- Detection by “gamma camera” or detector array
- (Image reconstruction)

From H. Graber, Lecture Note for BMI1, F05
Examples: PET vs. CT

- **X-ray projection and tomography:**
  - X-ray transmitted through a body from an outside source to a detector (transmission imaging)
  - Measuring anatomic structure

- **Nuclear medicine:**
  - Gamma rays emitted from within a body (emission imaging)
  - Imaging of functional or metabolic contrasts (not anatomic)
    - Brain perfusion, function
    - Myocardial perfusion
    - Tumor detection (metastases)

From H. Graber, Lecture Note, F05
Atomic Structure

- An atom = \{a nucleus, electrons\}
- nucleons = \{protons; neutrons\}
- Nuclide: unique combination of protons and neutrons in a nucleus
- mass number $A = \#\text{ nucleons}$
- atomic number $Z = \#\text{ protons} = \#\text{ electrons}$
- An element is denoted by its $A$ and $Z$
  - Ex: $^{12}_{6}C$ or C - 12

Figure 4.1
Stable vs. Unstable Nuclides

• **Stable nuclides:**
  - # neutrons ~= # protons (A ~= 2Z) when Z is small
  - # neutrons > # protons when Z is large
• **Unstable nuclides (radionuclides, radioactive atoms)**
  - Likely to undergo radioactive decay, which gives off energy and results in a more stable nucleus
Line of Stability

- Nuclides divide into two groups:
  - Non-radioactive — i.e., stable atoms
  - Radioactive — i.e., unstable atoms

- “Line” of stability:

Stability depends on ratio $Z:N$
Isotopes, etc

- **Isotopes**: atoms with the same Z but different A
  - E.g. C-12 and C-11
  - Chemically identical
- **Isobars**: atoms with the same A but different Z
  - Different elements
  - E.g. Carbon-11 and boron-11
- **Isotones**: atoms with the same number of neutrons but different A
- **Isomers**: atoms with the same Z and A but with different energy levels (produced after gamma decay)
What is Radioactivity?

- Radioactive decay: rearrangement of nuclei to lower energy states = greater mass defect
- Parent atom decays to daughter atom
- Daughter has higher binding energy/nucleon than parent
- A radioatom is said to decay when its nucleus is rearranged
- A disintegration is a radioatom undergoing radioactive decay.
- Energy is released with disintegration.
Decay Modes

- Four main modes of decay:
  - alpha particles (2 protons, 2 neutrons)
  - beta particles (electrons)
  - positrons (anti-matter electrons)
  - isomeric transition (gamma rays produced)

- Medical imaging is only concerned with:
  - positrons (PET), and
  - gamma rays (scintigraphy, SPECT)
Alpha Decay

- Alpha decay: the nucleus emits a Helium-4 particle (alpha particle)
  - Alpha decay occurs most often in massive nuclei that have too large a proton to neutron ratio. Alpha radiation reduces the ratio of protons to neutrons in the parent nucleus, bringing it to a more stable configuration.
  - mostly occurring for parent with $Z > 82$

From: http://www.lbl.gov/abc/wallchart/chapters/03/1.html
Beta Decay

- Beta decay occurs when, in a nucleus with too many protons or too many neutrons, one of the protons or neutrons is transformed into the other.
- Mass number $A$ does not change after decay, proton number $Z$ increases or decreases.
- Beta minus decay (or simply Beta decay): A neutron changes into a proton, an electron (beta particle) and an antineutrino.

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html
Positron Decay

- Also known as Beta Plus decay
  - A proton changes to a neutron, a positron (positive electron), and a neutrino
  - Mass number $A$ does not change, proton number $Z$ reduces

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html
Mutual Annihilation after Positron Decay

- The positron later annihilate a free electron, generate two gamma photons in opposite directions
  - The two photons each have energy 511 KeV, which is the energy equivalent to the rest mass of an electron or positron
  - These gamma rays are used for medical imaging (Positron Emission Tomography), detected using a coincidence detection circuit
Gamma Decay (Isometric Transition)

- A nucleus (which is unstable) changes from a higher energy state to a lower energy state through the emission of electromagnetic radiation (photons) (called gamma rays). The daughter and parent atoms are isomers.
  - The gamma photon is used in Single photon emission computed tomography (SPECT)
- Gamma rays have the same property as X-rays, but are generated different:
  - X-ray through energetic electron interactions
  - Gamma-ray through isometric transition in nucleus

From: http://www.lbl.gov/abc/wallchart/chapters/03/3.html
Measurement of Radioactivity

- **Radioactivity**, $A$, # disintegrations per second

  \[ 1 \text{ Bq} = 1 \text{ dps} \]

  \[ 1 \text{ Ci} = 3.7 \times 10^{10} \text{ Bq} \]

  (orig.: activity of 1 g of 226Ra)

  Bq=Becquerel (1 decay/sec)
  Ci=Curie:

  *Naturally* occurring radioisotopes discovered 1896 by Becquerel
  First *artificial* radioisotopes produced by the Curie 1934 (32P)

  The intensity of radiation incident on a detector at range $r$ from a radioactive source is

  \[ I = \frac{AE}{4\pi r^2} \]

  A: radioactivity of the material; E: energy of each photon
Radioactive Decay Law

- $N(t)$: the number of radioactive atoms at a given time
- $A(t)$: is proportional to $N(t)$
  
  $$A = -\frac{dN}{dt} = \lambda N$$

  $\lambda$: decay constant

- From above, we can derive
  
  \[
  N(t) = N_0 e^{-\lambda t}
  \]

  \[
  A(t) = A_0 e^{-\lambda t} = \lambda N_0 e^{-\lambda t}
  \]

- The number of photons generated (=number of disintegrations) during time $T$ is

  \[
  \Delta N = \int_0^T A(t) dt = \int_0^T \lambda N_0 e^{-\lambda t} dt = N_0 (1 - e^{-\lambda T})
  \]
Half-Life

- Half-life is the time it takes for the radioactivity to decrease by \( \frac{1}{2} \).

**Half-life** \( t_{1/2} \) is defined by

\[
\frac{A_{t_{1/2}}}{A_0} = \frac{1}{2} = e^{-\lambda t_{1/2}}
\]

- It follows that

\[
t_{1/2} = \frac{0.693}{\lambda}
\]
Statistics of Decay

• The exponential decay law only gives the expected number of atoms at a certain time $t$.

• The number of disintegrated atoms over a short time $\Delta t \ll T_{1/2}$ after time $t=0$ with $N_0$ atoms follows Poisson distribution

$$
\Pr\{\Delta N = k\} = \frac{a^k e^{-a}}{k!}; \quad a = \lambda N_0 \Delta t;
$$

$\lambda N_0$ is called the Poisson rate.

Strictly speaking

$$a = N_0 (1 - e^{-\lambda \Delta t})$$

When $\lambda \Delta t$ is small, $e^{-\lambda \Delta t} \approx 1 - \lambda \Delta t$, $a = N_0 \lambda \Delta t$
Radiotracers: Desired Property

• Decay mode:
  – Clean gamma decay: do not emit alpha or beta articles
  – Positron decay: positron will annihilate with electrons to produce gamma rays

• Energy of photon:
  – Should be high so that photons can leave the body w/ little attenuation
  – Hard to detect if the energy is too high
  – Desired energy range: 70-511 KeV

• Half-life
  – Should not be too short (before detector can capture) or too long (longer patient scan time)
  – Minutes to hours desired

• Half-value-layer (HVL)
  – Thickness of tissue that absorbs half of the radioactivity produced
  – Should be around the dimension of the organ to be imaged

• Monoenergetic
  – Energy sensitive detectors can discriminate the primary photons from scattered ones.
Decay Process Examples

\(\alpha\) decay

\[
^{238}_{92}\text{U} \rightarrow ^{234}_{90}\text{Th} + ^{4}_{2}\text{He}, \quad T_{1/2} \approx 4.5 \times 10^9 \text{y}
\]

\(\beta^-\) decay

\[
^{234}_{90}\text{Th} \rightarrow ^{234}_{91}\text{Pa} + e^- + \nu_e, \quad T_{1/2} = 24.1 \text{d}
\]

\[
^1_0\text{n} \rightarrow ^1_1\text{H} + e^- + \nu_e, \quad T_{1/2} = 10.6 \text{m}
\]

\(\beta^+\) decay

\[
^{11}_6\text{C} \rightarrow ^{11}_5\text{B} + e^+ + \nu_e, \quad T_{1/2} = 20.38 \text{ m}
\]

\[
^{10}_6\text{C} \rightarrow ^{10}_5\text{B} + e^+ + \nu_e, \quad T_{1/2} = 19.2 \text{ s}
\]

\[
^{15}_8\text{O} \rightarrow ^{15}_7\text{N} + e^+ + \nu_e, \quad T_{1/2} = 122 \text{ s}
\]

\(e^-\) capture

\[
^{41}_{20}\text{Ca} + e^- \rightarrow ^{41}_{19}\text{K} + \nu_e, \quad T_{1/2} \approx 1 \times 10^5 \text{y}
\]

Most of these naturally occurring processes are not useful for medical imaging applications, with too long Half-time, too short HVL, too high energy.

They can be used as radiotherapeutic agents, if they can be targeted to tumors, to destroy diseased tissue and stops the cancer from proliferating.
Radionuclides in Clinical Use

- Most naturally occurring radioactive isotopes not clinically useful (long $T_{1/2}$, charged particle emission, alpha or beta decay)
- Artificial radioactive isotopes produced by bombarding stable isotopes with high-energy photons or charged particles

$$99^\text{Mo} \xrightarrow{T_{1/2}=2.5\text{d}} 99^{m}\text{Tc} + e^- + \bar{\nu}$$

From H. Graber, Lecture Note, F05
The Technetium Generator

- Can be produced from an on-site generator
  - $^{99}\text{Mo} \rightarrow ^{99}\text{mTc} \rightarrow ^{99}\text{Tc}$,

- Decay characteristics of $^{99}\text{mTc}$:
  - half life = 6.02h, $E=140$ KeV, HVL=4.6 cm

\[ ^{99}\text{mTc} \rightarrow ^{99}\text{Tc} \rightarrow ^{99}\text{Tc} + \gamma (140 \text{ keV}) \]

- Used in more than 90% of nuclear imaging
- More detail: see handout [Webb, sec. 2.5]
Radiopharmaceuticals

- Radionuclide is bound to pharmaceuticals that is specific to metabolic activities (cancer, myocardial perfusion, brain perfusion)
- Gamma emitter
  - $^{99m}$Tc-Sestamibi (myocardial perfusion, cancer)
  - $^{99m}$Tc-labeled hexamethyl-propyleneamine (brain perfusion)
- Positron emitters
  - $^{11}$C, $T_{1/2} = 20$ min $[^{12}$C ($p, pn$) $^{11}$C; $^{14}$N ($p, \alpha$) $^{11}$C]:
    - many organic compounds (binding to nerve receptors, metabolic activity)
  - $^{13}$N, $T_{1/2} = 10$ min $[^{16}$O ($p, \alpha$) $^{13}$N; $^{13}$C ($p, n$) $^{13}$N]:
    - NH$_3$ (blood flow, regional myocardial perf.)
  - $^{15}$O, $T_{1/2} = 2.1$ min $[^{15}$N ($p, n$) $^{15}$O; $^{14}$N ($d, n$) $^{15}$O]:
    - CO$_2$ (cerebral blood flow), O$_2$ (myoc. O$_2$ consumption), H$_2$O (myoc. O$_2$ consumption & blood perfusion)
  - $^{18}$F, $T_{1/2} = 110$ min $[^{18}$O ($p, n$) $^{18}$F; $^{20}$Ne ($d, \alpha$) $^{18}$F]:
    - 2-deoxy-2-$^{[18}$F]-fluoroglucose (FDG, neurology, cardiology, oncology, metabolic activity)

From H. Graber, Lecture Note, F05
Common Radiotracers

- **Gamma Ray Emitters:**
  - Iodine-123 (13.3 h, 159 keV)
  - Iodine-131 (8.04 d, 364 keV)
  - Iodine-125 (60 d, 35 keV) (Bad. Why?)
  - Thallium-201 (73 h, 135 keV)
  - Technetium-99m (6 h, 140 keV)

- **Positron Emitters:**
  - Fluorine-18 (110 min, 202 keV)
  - Oxygen-15 (2 min, 696 keV)

Thyroid function

Kidney function

Most commonly used

Oxygen metabolism
Summary of Physics

- Radioactive decay is the process when an unstable nuclide is changed to a more stable one
  - Four modes of decay, generating alpha particles, beta particles, positrons and gamma rays respectively
  - Medical imaging exploits positron decay and gamma rays
- Radioactivity follows an exponential decay law, characterized by the decay constant or the half-life
- Desired properties for radio tracers
- Common radiotracers in nuclear medicine
Overview of Imaging Modalities

• **Planar Scintigraphy**
  – Use radiotracers that generate gamma decay, which generates one photon in random direction at a time
  – Capture photons in one direction only, similar to X-ray, but uses emitted gamma rays from patient
  – Use an Anger scintillation camera

• **SPECT (single photon emission computed tomography)**
  – Use radiotracers that generate gamma decay
  – Capture photons in multiple directions, similar to X-ray CT
  – Uses a rotating Anger camera to obtain projection data from multiple angles

• **PET (Positron emission tomography)**
  – Uses radiotracers that generate positron decay
  – Positron decay produces two photons in two opposite directions at a time
  – Use special coincidence detection circuitry to detect two photons in opposite directions simultaneously
  – Capture projections on multiple directions

• **Will focus on SPECT and PET only**
SPECT Instrumentation

- Similar to CT, uses a rotating Anger camera to detect photons traversing paths with different directions
- Recent advances uses multiple Anger cameras (multiple heads), reducing scanning time (below 30 minutes)
- Anger cameras in SPECT must have significantly better performances than for planar scintigraphy to avoid reconstruction artifacts
A typical SPECT system

Fig. 9.1 A dual head system
Anger Scintillation Camera

- Absorb scattered photons
- Convert detected photons to lights
- Convert light to electrical currents
- Compute the location with highest activity
- Compare the detected signal to a threshold
- Absorb scattered photons
Collimators

(a) Parallel hole
(b) Converging hole (magnifies)
(c) Diverging hole (minifies)
(d) Pin-hole (2–5 mm)
Imaging Geometry and Assumption

- Lines defined by (parallel) collimator holes
- Ignore Compton scattering
- Radioactivity is $A(x, y, z)$
- Monoenergetic photons, energy $E$
Imaging Equation

- Photon fluence on detector is

\[
\phi(x, y) = \int_{-\infty}^{0} \frac{A(x, y, z)}{4\pi z^2} e^{-\int_{z}^{0} \mu(x, y, z'; E) dz'} dz
\]

- Depth-dependent effects from:
  - inverse square law, and
  - object-dependent attenuation

- Consequences:
  - Near activity brighter
  - Front and back are different
Planar Source

- \( A_{z_0}(x, y) \) has radioactivity on \( z = z_0 \)

\[
A(x, y, z) = A_{z_0}(x, y)\delta(z - z_0)
\]

- Detected photon fluence rate

\[
\phi(x, y) = A_{z_0}(x, y)\frac{1}{4\pi z_0^2} \exp\left\{-\int_{z_0}^{0} \mu(x, y, z'; E)\,dz'\right\}
\]

- Two terms attenuate desired result
  - inverse square law: constant for \((x, y)\)
  - \(\mu\): not constant for \((x, y)\)
Imaging Equation: $\theta = 0$

\[
\phi(z, \ell) = \int_{-\infty}^{R} \frac{A(x, y, z)}{4\pi(y - R)^2} \exp \left\{ - \int_{y}^{R} \mu(x, y', z; E) \, dy' \right\} \, dy
\]

Replace $x$ by $l$
Examples

• Example 1: Imaging of a slab
• Example 2: Imaging of a two-layer slab

• Go through on the board
General Case: Imaging Geometry

\[ x(s) = \ell \cos \theta - s \sin \theta \]
\[ y(s) = \ell \sin \theta + s \cos \theta \]
General Case: Imaging Equation
Approximation

- Bold approximations: ignore attenuation, inverse square law, and scale factors:

\[ \phi(\ell, \theta) = \int_{-\infty}^{\infty} A(x(s), y(s)) \, ds \]

- Using line impulse:

\[ \phi(\ell, \theta) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} A(x, y) \delta(x \cos \theta + y \sin \theta - \ell) \, dx \, dy \]

Under this assumption, A can be reconstructed using the filtered backprojection approach.
The reconstructed signal needs to be corrected!
Correction for Attenuation Factor

- Use co-registered anatomical image (e.g., MRI, x-ray CT) to generate an estimate of the tissue $\mu$ at each location
- Use known-strength $\gamma$-emitting standards (e.g., $^{153}$Gd (Webb, §2.9.2, p. 79) or $^{68}$Ge (§ 2.11.4.1, p. 95)) in conjunction with image data collection, to estimate $\mu$ at each tissue location
- Iterative image reconstruction algorithms
  - In “odd-numbered” iterations, treat $\mu(x,y)$ as known and fixed, and solve for $A(x,y)$
  - In “even-numbered” iterations, treat $A(x,y)$ as known and fixed, and solve for $\mu(x,y)$
- From Graber, Lecture Slides for BMI1,F05
Example 1

- Imaging of a rectangular region, with the following structure. Derive detector readings in 4 positions (A,B,C,D)

Do you expect the reading at B and D be the same? What about at A and C?
SPECT applications

- Brain:
  - Perfusion (stroke, epilepsy, schizophrenia, dementia [Alzheimer])
  - Tumors
- Heart:
  - Coronary artery disease
  - Myocardial infarcts
- Respiratory
- Liver
- Kidney

• From Graber, Lecture Slides for BMI1,F05
  • See Webb Sec. 2.10
PET Principle

- Positron emitters
- Positron annihilation:
  - short distance from emission
  - produces two 511 keV gamma rays
  - gamma rays 180° opposite directions
- Principle: detect coincident gamma rays
Annihilation Coincidence Detection

- Detect two events in opposite directions occurring “simultaneously”
- Time window is 2-20 ns, typically 12 ns
- No detector collimation is required
  - Higher sensitivity
Detected PET Events
Coincidence Timing

- Three classes of events
  - true coincidence
  - scattered coincidence
  - random coincidence

- Sensitivity in PET
  - measures capability of system to detect “trues” and reject “randoms”
A Typical PET Scanner
Combined PET/CT Systems

- CT: provides high resolution anatomical information
- PET: Low resolution functional imaging
- Traditional approach:
  - Obtain CT and PET images separately
  - Registration of CT and PET images, to help interpretation of PET images
- Combined PET/CT: Performing PET and CT measurements within the same system without moving the patient relative to the table
  - Make the registration problem easier
  - But measurement are still taken separately with quite long time lag
Imaging Equation

Probabilities photon reaching detectors:

\[ N^+(s_0) = N_0 \exp \left\{ - \int_{s_0}^{R} \mu(x(s'), y(s')); E \right\} ds' \]

\[ N^-(s_0) = N_0 \exp \left\{ - \int_{-R}^{s_0} \mu(x(s'), y(s')); E \right\} ds' \]

\[ N_c(s_0) = N_0 \exp \left\{ - \int_{s_0}^{R} \mu(x(s'), y(s')); E \right\} ds' \]

\[ \cdot \exp \left\{ - \int_{-R}^{s_0} \mu(x(s'), y(s')); E \right\} ds' \]

\[ = N_0 \exp \left\{ - \int_{-R}^{R} \mu(x(s'), y(s')); E \right\} ds' \]

\[ \varphi(l, \theta) = K \int_{-R}^{R} A(x(s), y(s)) \exp \left\{ - \int_{-R}^{R} \mu(x(s'), y(s')); E \right\} ds' \] ds = K \int_{-R}^{R} A(x(s), y(s)) ds \cdot \exp \left\{ - \int_{-R}^{R} \mu(x(s'), y(s')); E \right\} ds' \]

\[ A(x, y) \text{ and } \mu(x, y) \text{ can be separated!} \]
Attenuation Correction

- Corrected sinogram

\[ \phi_c(\ell, \theta) = \frac{\phi(\ell, \theta)}{K \exp \left\{ - \int_{-R}^{R} \mu(x(s), y(s); E) \, ds \right\}} \]

- \( \mu(x, y) \) found from CT (transmission PET)

- One can apply filtered backprojection algorithm to reconstruct \( A(x, y) \) from the corrected sinogram
- Difference from SPECT:
  - Attenuation correction much easier!
Reconstruction from Corrected Sinogram

- Convolution backprojection yields $A(x, y)$

\[
A_c(x, y) = \int_0^\pi \int_{-\infty}^{\infty} \phi_c(\ell, \theta) \tilde{c}(x \cos \theta + y \sin \theta - \ell) \, d\ell \, d\theta
\]
Example 2

• Imaging of a rectangular region, with the following structure. Derive detector readings in 2 paired positions (A-C, B-D)
PET resolution compared to MRI

- Modern PET ~ 2-3 mm resolution (1.3 mm)

From H. Graber, lecture slides for BMI1,F05
PET evolution

From H. Graber, lecture slides for BMI1,F05
PET applications

• Brain:
  – Tumor detection
  – Neurological function (pathologic, neuroscience app.)
  – Perfusion

• Cardiac
  – Blood flow
  – Metabolism

• Tumor detection (metastatic cancer)

• From H. Graber, lecture slides for BMI1,F05
• See Webb Sec. 2.11.7
PET Application: See and Hear

Marcus E. Raichle, M.D., Washington University School of Medicine in St. Louis

The PET scan on the left shows two areas of the brain (red and yellow) that become particularly active when volunteers read words on a video screen: the primary visual cortex and an additional part of the visual system, both in the back of the left hemisphere. Other brain regions become especially active when subjects hear words through ear-phones, as seen in the PET scan on the right.
Image Quality Consideration

- We will consider the following for scintigraphy, SPECT, and PET together
  - Resolution: collimator, detector intrinsic
  - Noise
  - SNR
- Read: Sec. 8.4 in Textbook
Relation between True Image and Reconstructed Image in SPECT/PET

- Approximation:

\[ \hat{f}(x, y) = f(x, y) \ast h(r) \]

- In SPECT, \( h(r) \) includes:
  - collimator and intrinsic resolutions
  - ramp filter window effect

- In PET, \( h(r) \) includes:
  - the positron range function
  - detector width effects
  - ramp filter window effect
Summary of Imaging Principles

• Three major imaging modalities:
  – Planar scintigraphy
  – SPECT
  – PET

• Principle of Anger camera: collimator, scintillation crystal, photomultiplier

• Imaging principles of planar scintigraphy and SPECT
  – Both based on gamma decay
  – Very similar to X-ray projection and CT, except for the attenuation factor
  – Practical systems mostly ignore the attenuation factor

• Imaging principle of PET:
  – Coincidence detection: detect two photons reaching two opposite detectors simultaneously (within a short time window)
  – Detected signal is the product of two terms, depending on the radioactivity $A$ and attenuation $\mu$ separately
  – Can reconstruct radioactivity more accurately if $\mu$ can be measured simultaneously

• Image Quality
Reference

- Prince and Links, Medical Imaging Signals and Systems, Chap 7,8,9.
- A. Webb, Introduction to Biomedical Imaging, Chap. 2
  - Sec. 2.5 for Technetium generation; Sec. 2.10, Sec. 2.11.7 for Clinical applications of nuclear medicine.

- Recommended readings:
  - M. Reivich and A. Alavi (Eds.), *Positron Emission Tomography* (A. R. Liss, NY, 1985).
Homework

• Reading:
  – Prince and Links, Medical Imaging Signals and Systems, Ch. 7, 8,9.
• Note down all the corrections for Ch. 7,8,9 on your copy of the textbook based on the provided errata.
• Problems from Chap 7,8,9 of the text book
  – P.7.4
  – P7.6
  – P7.7 (assume the energy of the photons is E)
  – P7.9
  – P9.4
  – Complete solution for example 1
  – Complete solution for example 2