Medical Imaging Positron Emission Tomography (Outline of Lecture 6)

Nuclear Medicine

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- Pathological conditions are initiated by a change in basic biochemistry of tissue.
- Detect these indicators by uptake of radioactive compounds (radio-pharmaceuticals).
- Abnormal tissue distribution of radio-pharmaceuticals \Rightarrow strong indicator of disease.

Positron Emission Tomography:







A. Basic Principles

- Radio-pharmaceuticals emit positrons, positron annihilates with an electron, two photons (511 KeV) travelling in opposite directions.
- Detect coincident pairs of photons, this defines the line along which the annihilation took place.
- Positron emitting isotopes ¹⁸F, ¹¹C, ¹⁵O, ¹³N produced in a synchrotron. Half-times 2min 110min.
- Rapid chemical synthesis of structural analogues of biologically active molecules: ¹⁵O labelled water, fluorodeoxyglucose (FDG), [¹⁸F]DOPA,...



B. Instrumentation



• Detectors:

- scintillation crystal: converts high energy photons into a shower of low energy photons (visible part of the spectrum), maximal count rates: 10^5 photons/second.
- photomultiplier tube: amplification up to 10^6 electrons per photo-electron.
- Planar ring of detectors
- Coincidence detection circuitry: measures coincident events by summing and thresholding logic pulses triggered by detector events.

C. Image reconstruction

We assume for the sake of simplicity:

- Travel distance of the positron before annihilation ≈ 0 .
- All measured coincidences are correct.
- Consider only those emissions which are actually detected by some detector pair.

Denotations:

- igle x(r) density of the radio-pharmaceutical in the voxel $r \in V$
- iglet s(d) number of coincidences detected in the tube $d \in D$
- Observation: $S(D) = \{s(d) \mid d \in D\}$
- Unknown: $X = \{x(r) \mid r \in V\}$





(1) Let λ denote the density of the r.p. in a voxel. How many emissions per unit of time we expect? Poisson distribution

$$p(k) = e^{-\lambda} \frac{\lambda^k}{k!}$$



(2) If an emission occurs in voxel $r \in V$, what is the probability that it will be detected by the tube $d \in D$?. Let us denote this probability by $\pi(d \mid r)$. These probabilities can be calculated by geometrical considerations. Clearly, $\sum_{d \in D} \pi(d \mid r) = 1$ holds.

(3) Let s(d, r) denote the number of emissions in voxel $r \in V$ detected by the tube $d \in D$. This quantity is also Poisson distributed.

We have therefore

$$p(s;x) = \prod_{r \in V} \prod_{d \in D} e^{-\pi(d|r)x(r)} \frac{\left[\pi(d \mid r)x(r)\right]^{s(d,r)}}{s(d,r)!}$$



We don't know s(d,r). But we know $S(d) = \{s(d) \mid d \in D\}$, where $s(d) = \sum_{r \in V} s(d,r)$.

Therefore solve the task

$$\sum_{s \in S(D)} p(s;x) = \sum_{s \in S(D)} \prod_{r \in V} \prod_{d \in D} e^{-\pi(d|r)x(r)} \frac{\left[\pi(d \mid r)x(r)\right]^{s(d,r)}}{s(d,r)!} \to \max_{x}$$

Expectation Maximisation Algorithm: Start with some initial estimate of x^0 . Then maximise iteratively

E-step Given the current estimate of $x^{(t)}$, calculate an estimate for s(d, r):

$$s(d,r) \approx \mathbb{E}\left[s(d,r) \mid s(D), x^{(t)}\right]$$

M-step Given the estimate for s(d, r), re-estimate x:

$$x^{(t+1)} = \arg\max_{x} p(s;x)$$





Joining both steps gives the update formula

$$x^{new}(r) = x(r) \sum_{d \in D} \frac{s(d)\pi(d \mid r)}{\sum_{r' \in V} x(r)\pi(d \mid r)}$$

D. Clinical applications

- Brain imaging
 - Measuring regional cerebral blood flow: use $^{15}\mathrm{O}\text{-labelled}$ water
 - Measuring tissue metabolism: use FDG which passes BBB, enter cells, phosphorylates, is trapped in the cell
 - Measure the rate of dopamine synthesis: use $[^{18}F]DOPA$





- Cardiac studies
 - Measure blood flow: use ${}^{13}NH_3$.
 - Measure metabolism: use FDG
- Tumor and metastatic cancer diagnosis
 - Measure metabolism (e.g. whole body scan): use FDG.





