How to read and make sense of the literature

(advice from Cindy Jordan)

How to get started?

Start with

recent review articles

(“**recent”** means within the last 5 years, preferably within the last two)

Why?

What are the advantages?

- Gives you the big picture
- Usually well written by leaders in the field
- Tells you who the main players are
  - By reading a few reviews, you can quickly gain a sense for who the main players are
- Provides a “road map” for additional reading
  - lots of citations that guide you to the relevant seminal primary reports

How to find review articles?

Use **PubMed**

Key words: “review” and “topic of interest”

What are good sources to start with?

- Current Opinions…(Neurobiology)
- Trends in…(Neuroscience)
- Commentaries in scientific journals

Advantages

- Written by leaders in the field
- Usually easy to read, relatively short, good schematics, available on line, and targeting readers who are looking for an introduction to or an update on a topic that might be somewhat peripheral to their own area of expertise (*that's you!)*
- Commentaries gives you the latest and greatest and relevant background all in 1-2 pages.
- Reference section provides main messages for many key citations

"*Current Opinions*…" notes particularly important citations with asterisks and gives you the main message in the bibliography

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Huang EJ, Reichardt LF: **Neurotrophins: roles in neuronal development and function.** *Annu Rev Neurosci* 2001, **24**:677-736.
2. Sofroniew MV, Howe CL, Mobley WC: **Nerve growth factor signaling, neuroprotection, and neural repair.** *Annu Rev Neurosci* 2001, **24**:1217-1281.
3. Kaplan DR, Miller FD: **Neurotrophin signal transduction in the nervous system.** *Curr Opin Neurobiol* 2000, **10**:381-391.
4. Ehlers M, Kaplan D, Price D, Koliatsos V: **NGF-stimulated retrograde transport of TrkA in the mammalian nervous system.** *J Cell Biol* 1995, **130**:149-156.
5. Riccio A, Pierchala BA, Ciarallo CL, Ginty DD: **An NGF–TrkA-mediated retrograde signal to transcription factor CREB in sympathetic neurons.** *Science* 1997, **277**:1097-1100.
6. Senger DL, Campenot RB: **Rapid retrograde tyrosine phosphorylation of TrkA and other proteins in rat sympathetic neurons in compartmented cultures.** *J Cell Biol* 1997, **138**:411-421.
7. Tsui-Pierchala BA, Ginty DD: **Characterization of an NGF–P-TrkA retrograde-signaling complex and age- dependent regulation of TrkA phosphorylation in sympathetic neurons.** *J Neurosci* 1999, **19**:8207-8218.
8. Watson FL, Heerssen HM, Moheban DB, Lin MZ, Sauvageot CM, Bhattacharyya A, Pomeroy SL, Segal RA: **Rapid nuclear responses to target-derived neurotrophins require retrograde transport of ligand–receptor complex.** *J Neurosci* 1999, **19**:7889-7900.
9. Beattie EC, Zhou J, Grimes ML, Bunnett NW, Howe CL, Mobley WC: **A signaling endosome hypothesis to explain NGF actions: potential implications for neurodegeneration.** *Cold Spring Harbor Symp Quant Biol* 1996, **61**:389-406.
10. •• Weible MW II, Bartlett SE, Reynolds AJ, Hendry IA: **Prolonged recycling of internalized neurotrophins in the nerve terminal**

(Erk1/2) only for local signaling and relies on the Erk5 pathway for retrograde signaling and survival. In contrast, neurotrophin stimulation of cell bodies utilizes both the classic MAPK pathway and the Erk5 pathway.

18. Wu C, Lai CF, Mobley WC: **Nerve growth factor activates persistent Rap1 signaling in endosomes.** *J Neurosci* 2001, **21**:5406-5416.
19. Reynolds A, Bartlett S, Hendry I: **Signalling events regulating the retrograde axonal transport of ^{125}I-β nerve growth factor *in vivo*.** *Brain Res* 1998, **798**:67-74.
20. •• Yano H, Lee FS, Kong H, Chuang J, Arevalo J, Perez P, Sung C, Chao MV: **Association of Trk neurotrophin receptors with components of the cytoplasmic dynein motor.** *J Neurosci* 2001, **21**:RC125.

The authors demonstrate that Trk receptors bind directly to a dynein light chain. *In vivo*, Trk receptors are associated with this and other dynein constituents. Following nerve ligation, dyneins and Trks accumulate in the distal segment. These data provide support for dynein-based transport of Trk-containing vesicles.

21. Oiwa K, Takahashi K: **The force–velocity relationship for microtubule sliding in demembranated sperm flagella of the sea urchin.** *Cell Struct Funct* 1988, **13**:193-205.
22. •• MacInnis B, Campenot R: **Retrograde support of neuronal survival without retrograde transport of nerve growth factor.** *Science* 2002, **295**:1536-1539.

Here, MacInnes and Campenot use NGF linked to microspheres to prevent the internalization of NGF into vesicles. They demonstrate that NGF linked to beads and applied selectively to distal axons is capable of inducing neuronal survival. This suggests the existence of non-vesicular retrograde mechanisms for survival.

23. Hempstead BL, Rabin SJ, Kaplan L, Reid S, Parada LF, Kaplan DR: **Overexpression of the Trk tyrosine kinase rapidly accelerates nerve growth factor-induced differentiation.** *Neuron* 1992, **9**:883-896.
24. Berninger B, Garcia DE, Inagaki N, Hahnel C, Lindholm D: **BDNF and NT3 induce intracellular Ca^{2+} elevation in hippocampal neurones.** *Neuroreport* 1993, **4**:1303-1306.
25. Zirrgiebel U, Lindholm D: **Constitutive phosphorylation of TrkC receptors in cultured cerebellar granule neurons might be**

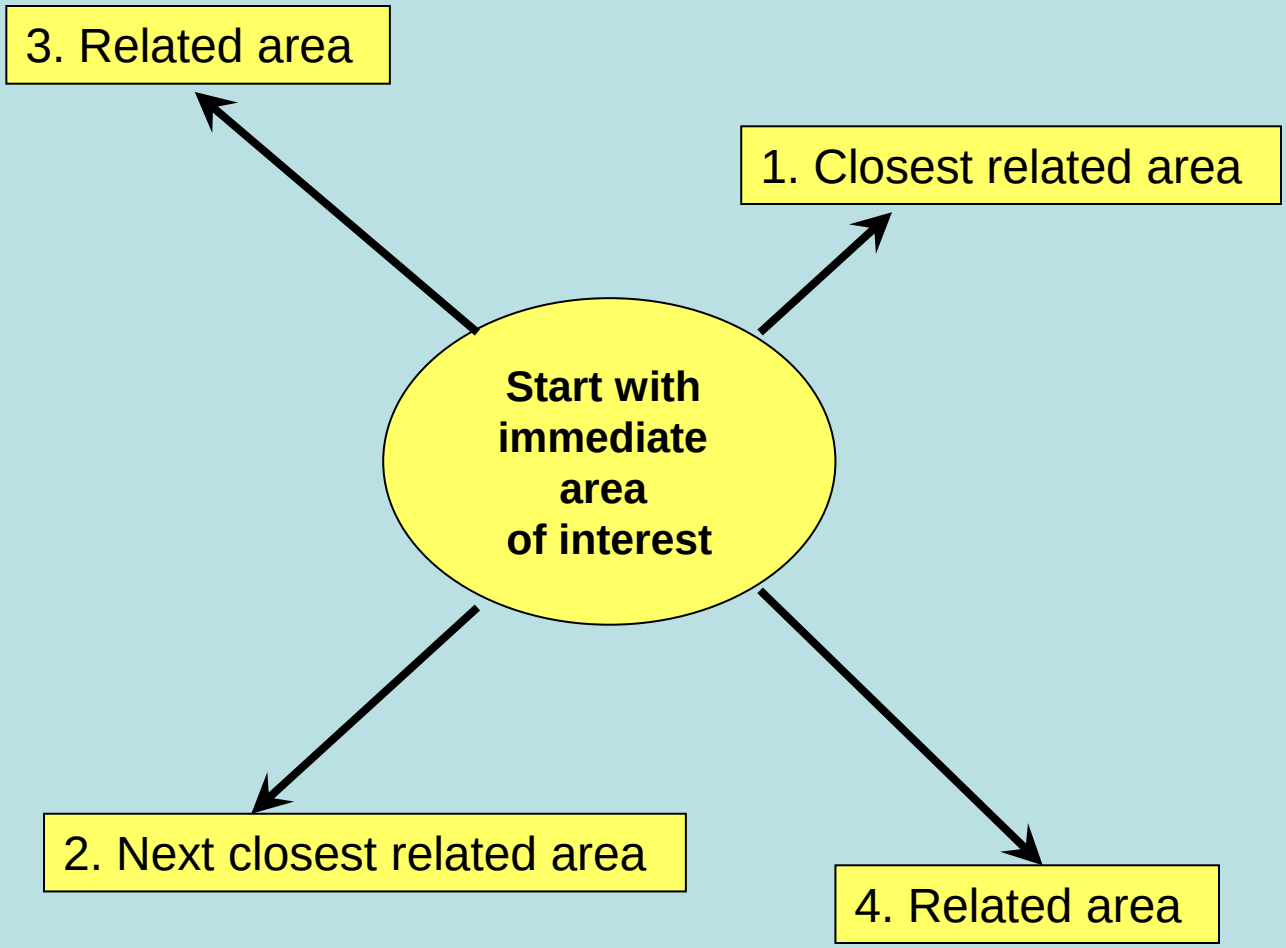
More substantive reviews

- Nature Reviews: Neuroscience
- Annual Reviews in Neuroscience
- Nature, Science, Cell, Neuron, etc

Select reputable, well known journals!

Constrain your reading

(start slow…)



Getting broader and “seeing” connections between various subfields as you read

As you read…

build a picture or story in your head

…try to “connect the dots” between data from different papers

How to keep track?

Establish a bibliographic data base for keeping track of and organizing your papers (e.g., Endnote)

- Can easily search in your data base
- Can easily generate a bibliography (for your dissertation, publications, grant proposals, etc. *even for your comp exams!!*)

Word of caution: back-up your Endnote file
(thumb drive, CD, cyberspace…)

Other resources…

- **Web of science** *(you can link via the MSU library)*
  - If you find a particularly good/relevant paper and you want to find other papers relevant to that one and that build on reported finding, then use **“cited reference search”** (one of the options on the top menu)

How to read a paper?
It depends…

- Review articles: read the entire paper starting at the beginning (unless you see that there are only discrete sections that are pertinent)
- Primary reports: start w/ the title and the abstract
  - *Info on next slide tells you why reading and digesting information in the abstract is worthwhile*
  - *A good title should provide the ultimate main message of the study's results*
- then look at the figures and read the captions…
- then if judged relevant and interesting, the results, etc…

What is in an abstract?

- **Main question**
- **Rationale** (why the question was asked)
  - which automatically means background information is given
- **Methods** (what was done to answer the question)
- **Main results and conclusions** (what was found and what it all means, from the viewpoint of the authors)

In short, if an abstract is well written:

You should learn enough about the paper to know whether it is worth reading

Don’t forget to back up regularly

Good Luck