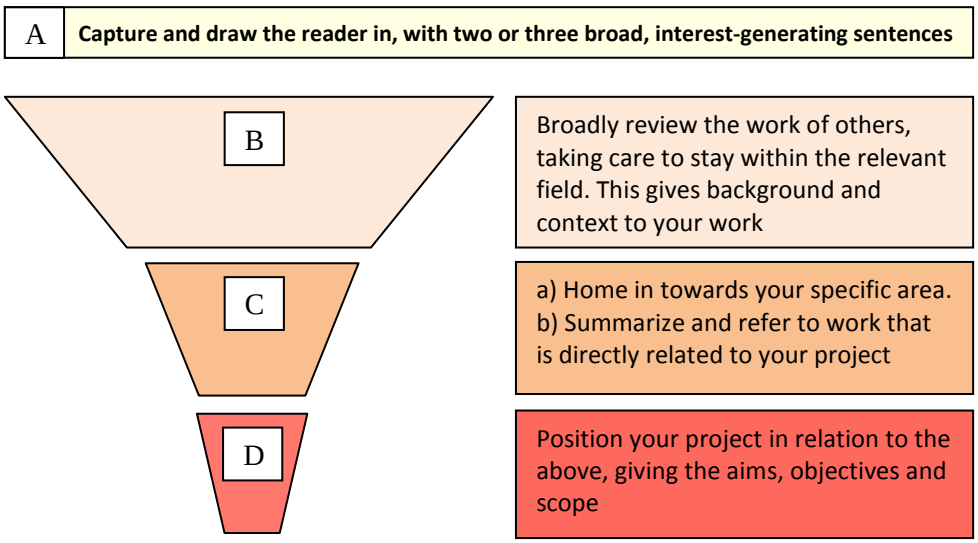
5 Steps to writing your Introduction

The introduction is the beginning of your manuscript/article and sets the scene. This is where you refer to the work of other researchers and their publications and also position and introduce your work in relation to this.

Format of an introduction to a scientific paper

Although every introduction is different, good introductions follow a similar structure:



e.g. *"x is an important issue … because it affects …"*

e.g. *"there have been a number of studies considering … author a found … author c, d. e …"*

e.g. *"little is known about how z affects x … and its role in … Author f touched on …. when she … and author g …"*

e.g. *"Here we demonstrate how z behaves in … and specifically measure … and … These findings have relevance to … and x"*

A good introduction:

- **"Opens"** the paper and generates interest
- **Uses keywords** from the title in the first one or two sentences
- Provides a **background** for the reader by describe existing, relevant, peer-reviewed publications in the field ... hence putting the work in context.
- Draws on an 'appropriate' number of references. You need to demonstrate that you have **knowledge of the work of key players** in the area
- **Starts broad** within the research area.
- **Explains** relevant, underpinning scientific principles to support the reader and enable understanding. However, don't try to include all explanations/thoughts in the Introduction, some may be more relevant to the Discussion section (see "5 steps to writing your Discussion")
- **Focuses** on and **summarises** work directly relevant to, or that has led up to, your project
- Includes your specific **research question** and relates it to the existing published work
- Includes **your aim** (broad) and highlights the gap in knowledge that you aim to address
- States **specific objectives/outcomes** that enabled you to work towards or achieve your aim (what did you set out to do/measure/observe?)
- States the **scope** of the project
- Says **why your work is important or of current interest**
- Supports all statements by **in-text citations** (which must be appropriately referenced according the style of the target journal)

How many references?

… it depends!

- on the subject area and the type of article you are writing (doctorate thesis, novel research article, review article, undergraduate project …). Discuss with your supervisor.

You need to demonstrate that you have read around the subject and have identified and understood important and relevant work in the area. There may indeed be a lot of work, in which case you need to be selective and choose the most relevant and interesting, and more recent. Equally, there may be only limited work in the area, so you may need to go back further (in date) and search widely. Whichever is the case, be sure to include work by known key researchers in the area – to omit these will limit your chances of publication.

Perhaps, as a general guide, 20 – 30 primary research articles from peer reviewed journals would be reasonable. Make sure you come right up to date and include the most recent work performed on the topic.

Read the introduction from the paper below and answer the questions that follow

The following activity relates to this article published in the *Journal of Pharmacology and Experimental Therapeutics:*

"Lymphatic Absorption Is the Primary Contributor to the Systemic Availability of Epoetin Alfa following Subcutaneous Administration to Sheep"
http://jpet.aspetjournals.org/content/313/1/345.full

1. Erythropoietin (EPO) is a renally synthesized 30.4-kDa glycoprotein involved in the regulation of red blood cell proliferation and differentiation. Recombinant human epoetin alfa (rHuEPO) has been extensively utilized in the treatment of anemia associated with chronic renal failure, AIDS, and chemotherapy.

2. Pharmacokinetic studies of rHuEPO have demonstrated dose-dependent disposition in humans (Flaharty et al., 1990; Veng-Pedersen et al., 1995), monkeys (Ramakrishnan et al., 2003), sheep (Veng-Pedersen et al., 1999), and rats (Kato et al., 1997) after i.v. administration. In these studies, nonlinear kinetics were characterized by decreased clearance with increasing dose. Although the exact elimination pathway has not been fully elucidated, studies comparing clearance (CL), mean residence time (MRT), and terminal half-life ($t_{1/2}$) pre- and postablation of the bone marrow in sheep, have provided significant evidence that elimination occurs predominantly in the bone marrow (Chapel et al., 2001). The capacity-limited CL is likely to be a receptor-mediated endocytosis by erythroid progenitor cells and has been described previously using a Michaelis-Menten-type elimination (Kato et al., 1997; Veng-Pedersen et al., 1999; Ramakrishnan et al., 2003). Although EPO receptors appear to have an important role in the distribution of EPO outside the central compartment (Chapel et al., 2001), dose-related changes in volume of distribution at steady state (V_{ss}) have not been observed in rats (Kato et al., 1997) suggestive of a nonsaturable distribution process (Veng-Pedersen et al., 1999).

3. Absorption of rHuEPO after s.c. injection is slow and prolonged with the time to maximal concentration (T_{max}) occurring between 10 and 18 h in humans (Kampf et al., 1989; Jensen et al., 1994). Reported bioavailability estimates are low and variable, ranging from 18 to 49%; however, these original noncompartmental bioavailability assessments have not taken into account the effects of nonlinear clearance (Boelaert et al., 1989; Kampf et al., 1989; Salmonson et al., 1990; Halstenson et al., 1991). The large molecular size of rHuEPO has been suggested to impede absorption from the s.c. injection site (Macdougall et al., 1991) based on the negative correlation previously observed between the molecular size and bioavailability of heparins (Emanuele and Fareed, 1987). Despite the apparent low bioavailability, s.c. administration of rHuEPO produces equivalent efficacy to i.v. administration, and this is assumed to be due to the prolonged absorption leading to reduced receptor saturation (Kampf et al., 1989; Bommer et al., 1991). Absorption rates of rHuEPO vary according to the administration site, most likely reflecting regional differences in blood and lymph flow

(Jensen et al., 1994).

4. The lymphatics are thought to be the primary route of absorption from the s.c. injection site for protein therapeutics greater than about 16 kDa due to restricted vascular access afforded by the continuous endothelial layer of blood capillaries (Supersaxo et al., 1990; Porter and Charman, 2000; McLennan et al., 2003). The intercellular junctions within the lymphatic vessel wall create cleft-like openings that provide an alternative pathway from the interstitium into the lymph and indirectly into the systemic circulation via the thoracic duct (Leak, 1976). The relative roles of the blood and lymphatic absorption pathways after s.c. administration has been directly assessed using lymph cannulated animal models for a number of therapeutic proteins including interferon α-2a (Supersaxo et al., 1990), human growth hormone (Charman et al., 2000), insulin (Charman et al., 2001), and rmetHu-Leptin (McLennan et al., 2003). Collectively, the importance of the lymphatics in the absorption and systemic availability of proteins has been demonstrated by the recovery of a high proportion of the administered protein dose (17-62%) in peripheral lymph draining the s.c. injection site.

5. Absorption of rHuEPO into lymph has been previously measured in a thoracic duct cannulated rat model, although because lymph was sampled at discrete intervals as opposed to continuous collection, the extent of rHuEPO absorption via the lymphatics could not be quantified (Moriya et al., 1997). The lymphatics have also been implicated as a significant absorption pathway by pharmacokinetic modeling of serum concentrations in monkeys, which identified a slow absorption process for approximately 65% of the absorbed dose that was attributed to lymphatic uptake (Ramakrishnan et al., 2003).

6. The objective of this study was to quantify the contribution of the lymphatics to the absorption and systemic availability of rHuEPO following s.c. injection. The nonlinearity of rHuEPO after i.v. administration in sheep was assessed at different dose levels, and a compartmental model was developed to estimate bioavailability. Given the low reported bioavailability of rHuEPO in the literature, an additional aim was to investigate the potential for clearance during transport through the lymphatics contributing to a reduction in bioavailability

Look at the opening paragraph 1. and consider the following: a) Do you think it adheres to our format (on page 1) and starts as we propose (with "A")? b) Highlight where the authors put the work in context and show the reader the 'real-life' applications. c) Identify any key words used in both the title and in the opening paragraph.	
Which paragraph would you describe as "scene-setting"?	
Which paragraph introduces the area and problem that this study sets out to consider/address (i.e. stage "C a)" in our proposed format)?	
Which paragraph explains the underpinning science to the reader?	
Which paragraph mentions directly relevant research (i.e. stage "C b)") that leads in to their specific project (stage "D")?	
Paragraph 6. explains what this study sets out to do. Highlight: a) The overall aim b) The 2 main project outcomes	
How many publications did the authors cite in their introduction?	

5 steps to develop your introduction

[NOTE, this makes the assumption that you have already conducted an extensive literature review]

		✓
Each step relates to our proposed format of an introduction on page 1, and the four stages A to D		
STEP **1**	**Identify and organize the CONTENT – Stages A – C** **a) CONTEXT** - identify the broad, day-to-day area/challenge that relates to your project **b) IDENTIFY** i) Start with all the papers from your literature review ii) Identify key researchers that you must include? iii) Identify the papers you want to reference, categorize each as relevant to each of: - Stage B; - Stage C a); - Stage C b) iv) Highlight the specific aspect of each paper identified that you want to include v) Identify any underpinning science/procedures/principles that warrant explanation. (Make sure you understand them yourself and then work-up your explanation for your introduction and do this clearly and succinctly) [NOTE – revisit the literature for any recent publications]	
STEP **2**	**LINK – Stages C b) to D** Focus on work that is directly related to your project (stage C b)): a) Identify how your work supports or contradicts it b) Identify how your project contributes to what has gone before .... write this down!	
STEP **3**	**WRITE – draft your introduction** a) Produce a **diagram** outlining your introduction and the content of each Stage (A to C) b) **Start writing -** piecing together your work from STEPs **1** and **2** Aim for 2000 – 3000 words initially.	
STEP **4**	**DESCRIBE – Stage D** Write the final paragraph (to add to the end of your draft intro., STEP **3**) that : a) links to STEP **2** b) states your over-arching project aim c) describes your specific outcomes or measures d) defines the scope of your project	
STEP **5**	**EDIT** Give yourself time between STEP **4** and this final STEP **5** before you return to your draft: a) Edit and cut it back to an appropriate word count (~30% of the total article word count b) ~1500 - 1800 words as a guide) c) Does it read well? – check grammar, spelling and readability. d) Refine and ask at least 3 colleagues to read it and comment e) Check all your citations and references	