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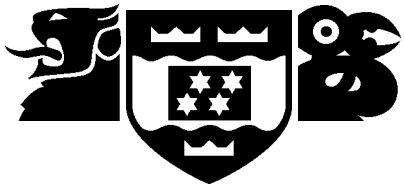

Department of Computer Science

PO Box 600
Wellington
New Zealand

Tel: +64 4 471 5328
Fax: +64 4 495 5232
Internet: Tech.Reports@comp.vuw.ac.nz

Automated analysis of x-ray angiograms

Peter Hall

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Abstract

An angiogram is an image of the blood vessels, and such images can be acquired via x-ray or magnetic resonance imaging. This paper discusses problems that arise when attempting quantitative x-ray angiography on a computer. Standard solutions are presented where they exist and we include proposals of our own. In particular, we focus upon the problem of reconstructing the three-dimensional network formed by blood vessels, from only a few x-ray angiograms. Our solution to this depends upon successful integration of methods drawn from computer graphics, computer vision, an anatomical model, and machine learning.

Author Information

Peter Hall is a lecturer at Victoria University. His principal research interests are scientific visualisation, and computer vision.

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P.M. Hall
Department of Computer Science
P.O. Box 600
Victoria University of Wellington
Wellington
New Zealand

R. Feltham, T. Fitzjohn
Wakefield Radiology
P.O. Box 7168
Wellington
New Zealand

Abstract

An angiogram is an image of the blood vessels, and such images can be acquired via x-ray or magnetic resonance imaging. This paper discusses problems that arise when attempting quantitative x-ray angiography on a computer. Standard solutions are presented where they exist and we include proposals of our own. In particular, we focus upon the problem of reconstructing the three-dimensional network formed by blood vessels, from only a few x-ray angiograms. Our solution to this depends upon successful integration of methods drawn from computer graphics, computer vision, an anatomical model, and machine learning.

Key words and Phrases

X-ray angiography, image processing, vision processing, computer graphics, anatomical model, machine learning.

1 Introduction

Angiograms are images of blood vessel structures (*vasculature*) that are acquired using either magnetic resonance imaging or x-ray methods. Angiograms are acquired not only for diagnosis but also for treatment planning, where accurate delineation of any lesion and information concerning its blood supply is important. Typical features that clinicians look for in angiograms include the number and position of feeding vessels (*arteries*) as well as the way in which blood is drained from the lesion. Very often the presence of abnormal or unusual vessel structure, position or geometry may be the only clue to the existence of an abnormality. Some types of lesion are associated with a specific vascular structure. Furthermore quantitative information concerning vasculature is of considerable assistance in planning interventional therapy, such as when small tubes or catheters are inserted into the blood system and placed within the feeding vessels to release small amounts of sclerosant or mechanical obstructing devices. Under these circumstances intimate knowledge of vessel diameter, course, and curvature is essential.

Quantitative information of this kind is present in angiograms and should be accessible via a computer. In this paper we are concerned with automated analysis of x-ray angiograms for a variety of medical applications. Automatic methods are desirable because they bring the advantages of

objectivity and precision over manual methods. In particular, we will be concerned with analysing x-ray angiograms with the intention of producing a three dimensional reconstruction of the vasculature.

X-ray angiography yields perspective images of vasculature. Blood does not naturally absorb sufficient x-rays for the vessels to be easily visible, so a contrast agent is injected into the blood flow. This makes it an invasive technique and causes considerable discomfort and risk to the patient. Because of this, and the desire to reduce exposure to x-rays, angiography obtains a limited number of images from a few points of view, usually two. Typically these points of view are from the back (*posterior-anterior*) and from the side (*lateral)*. In this case the pair of images obtained are separated by an angle of about 90° and are called *biplane angiograms*. At other times the angiograms may be separated by only a few degrees, 4° say. In this case the pair of images are called *stereo-angiograms*. Images from other angles are sometimes obtained, such as the *Townes projection*, that views the vasculature from forehead to the nape of the neck. From any given point of view x-ray angiography produces a time sequenced set of images called *cine-angiograms.* These show the positions of contrast agent at different time instants as it moves through the blood stream. Each distinct position is called the *phase* of the contrast agent. Three phases are of particular interest: the *arterial phase*; the *venous phase*; and the *capillary phase*. The arterial phase refers to the blood vessels that lead from the heart. The venous phase refers to blood vessels that lead to the heart. The capillary phase consists of narrow blood vessels that connect the arterial phase to the venous phase. Each set of cine-angiogram views is usually acquired independently from all others; the x-ray machine is moved into a new position between their capture, and a separate injection of contrast agent is required each time.

Magnetic resonance angiography (MRA) is the most modern of the acquisition methods. MRA is a non-invasive technique, a desirable characteristic from a medical point of view. MRA images can be simultaneously obtained from many angles, which is desirable from a computational point of view, especially for three-dimensional reconstruction purposes. However, MRA is more expensive and less widespread than x-ray angiography. Moreover, even though recent advances in MRA allow it to demonstrates the three main phases of blood flow (see Edelman *et al*., 1983) it fails to do so with the fine resolution that x-ray angiography is capable of. MRA is also susceptible to flow rate artefacts that can give rise to spurious phase information. Consequently, we choose to analyse x-ray angiograms in the first instance.

Automated analysis of angiograms requires their capture as digital images. The next section, section 2, discusses the source of artefacts introduced during image capture and methods for their removal. Analysis of clinically interesting features within the angiograms can then proceed. Image analysis procedures that enable these features to be measured in angiograms are outlined in section 3. Three dimensional reconstruction of vasculature is discussed in section 4, and section 5 concludes the paper.

2 Analysing x-ray angiograms

The highest quality digital x-rays are produced via a *radiological image intensifier* (RII) that converts x-rays into digital images. The RII is a photo-electric device that yields images with an improved contrast, but unfortunately introduces a non-linear warping effect called *pin-cushion distortion*. This means that each point in the image is moved away from the centre of projection by

an amount proportional to its distance to the centre of the projection. Unwarping images from an RII is a two stage process. First the amount of distortion must be calibrated so that a mapping between distorted and un-distorted images is established. A grid of squares is often used for this. Some researchers use the distorted image of the grid to fix parameters in a model of the action of the RII device (see Lavayssier *et al*., 1987). We choose to fit a set of quadratic curves to the lines in the grid's image, see Hall *et a*l. (1993) for details. In the second stage of unwarping the mapping is used to correct the distortion. Because the amount of distortion is a function of position a spatially variant filter must be used during correction, see Hall *et al*. (1993) for details.

As discussed above, the injection of contrast agent artificially raises the x-ray absorbing power of the blood to a level sufficient for them to be visible. However, other objects, such as the bones, are composed of material that absorb x-rays naturally and so the vasculature appears against a background of these objects. These unwanted objects can be removed by acquiring an image before the contrast agent is injected, this is called a *subtraction mask*. The mask image is subtracted from each of the angiograms taken from the corresponding point of view and the result should be a clearly defined vasculature. This process is called *digital subtraction angiography* (DSA). However, the patient may move between the time the mask is taken and the time the sequence of angiograms with contrast agent is taken. When the angiograms are of vasculature surrounding the heart most of this movement is caused by the beating heart. Any movement results in unwanted artefacts on the DSA image. The removal of such artefacts has been investigated by Leclerc and Benchimol (1987) and also by Van Tran and Sklansky (1992). Their methods involve warping the image in a non-linear fashion.

Image warping because of the capture device and patient movement are the primary sources of unwanted artefacts in angiograms. Other sources of noise exist, quantum mottle for example. These can be dealt with by standard image processing methods and so we turn our attention to the measurement of clinically interesting features within angiograms.

3 Measuring clinically interesting features

A stenosis is the narrowing of the internal cross-sectional area of a vessel. Such narrowing can occur because of calcium and cholesterol deposits sticking to the blood vessel wall. Stenoses are clinically significant because blood flow can be severely restricted to the target organ. Stenoses are detectable by an unexpected change in vessel width. Manual attempts at measuring vessel widths have proven unreliable, as documented by DeRouen *et al.* (1977), Brown *et al.* (1982). Width measurement is complicated by a number of reasons: the amount of x-rays absorbed by an x-ray varies over a cross-section; they are curved, three-dimensional, objects; angiograms are perspective projections. Attempts at automatic measurement have been made. The variability of x-ray absorption over the cross-section leads to a gradual rather than step-wise changes of gray level values in angiograms. Consequently determining the edges of vessels requires care. Kitamura *et al.* (1988) use a model that assumes an elliptical cross-section to assist width estimation. Barba *et al*. (1987) use an iterative algorithm that yields crescent-shaped cross-sections. Levin (1992) suggested examining a line through the cross-section for inflection points. Since angiograms are perspective projections the measured width will be related to the actual width by a scale factor that will be unknown in general. Fencil *et al.* (1987) use stereo-angiograms to estimate this factor.

Vessel trajectory can be important. For example, a pre-shaped catheter can simplify treatment

planning during *angioplasty*, a technique where stenoses are dilated from within the vessel by an inflatable balloon. Determination of three-dimensional vessel trajectories is especially useful and this aim motivates part of our current research. Tracking vessels seems to be the standard method for segmenting them from angiograms, though Coppini *et al.* (1993) provides an exception. All tracking methods reported so far seem to require the user to initiate tracking by marking a starting point. Tracking vessels requires a reliable width estimate to be found. Working with a single image Hoffman *et al*. (1986, 1987) use a pair of square boxes to decide in which direction the tracker should step next. The size of inner box is of the same order as the estimated vessel width, and the outer box is double this. An examination of the image intensity values around the periphery of the inner box is used to estimate the next step. The outer box is used to resolve any conflicts that may arise. Levin (1992) points out that the square box is a non-isotropic operator and replaces it with a circle, which is isotropic. The circle automatically adapts to estimated vessel width. Kitamura *et al.*, (1988) track vessels in three-dimensions by simultaneously tracking a pair of projections. Vessel tracking is difficult because vessels furcate and their images often overlap in complicated ways. Recovering the blood vessel network accurately requires information a priori to the projections, and this issue is taken up in more detail in section 4, below.

Blood flow measurement is clinically useful because it can give some indication as to the nature of the abnormality or severity of the stenosis, as well as providing an index of treatment progress. Methods for estimating blood flow rates through vessels have been investigated. This is a very difficult task because of the large number of variables that include: initial impetus of contrast agent at injection; the time profile of concentration of contrast agent as it is released into the blood flow; and the pulsatile nature of blood flow; also the elastic nature of blood vessel walls. Methods based on mass preservation have influenced early studies, Zierler (1962) and later studies, Marins *et al.* (1990). Time-density methods measure the arrival of some part of the bolus of contrast agent (Zierler 1962, Rosen and Silverman, 1973, Fermor *et al.* 1979, Close *et al.* 1992). Unfortunately, these have proven inaccurate. Distance-density approaches have met with greater success (Hoffman *et al.*, 1991). However, because flow occurs in three dimensions any estimate of it based on two-dimensional information alone will generally be erroneous. This point is made by Fencil *et al.* (1989) who use stereo-angiography in an attempt to measure flow rate in three dimensions. One outstanding problem which seems to have been ignored in the literature is that of matching the position of the contrast agent in the vasculature between separate sets of cine-angiograms. This must be accounted for when reconstruction in three dimensions, as Hall and Walton (1993f) report. There a solution to the problem is not suggested, rather it is circumvented by integrating the cine-angiograms into a single image.

Detection of stenoses is usually limited to the vasculature that surround the heart and the *carotid arteries* leading to the brain. Vasculature in the brain may also have malformations such as an *arterio-venous malformation* (AVM). An AVM is a tangled web of blood vessels that develops within the growing brain and acts as a short circuit between the arteries and veins. These AVMs are dangerous - haemorrhage can be fatal. Researchers such as Kountanis and Kountanis (1987) have developed expert systems that detect abnormalities in radiographs of the brain. Even so, to the best of our knowledge we have conducted the only investigation into segmenting AVMs from angiograms (Hall *et al.*, 1993a). Our method assumes that the image of an AVM is approximately circular when compared to long and sinuous blood vessels. It uses row and column sums of the angiogram to locate a single point on the AVM, and then determines its border via region-growing

and constraint minimisation methods. Reconstruction of AVMs in three dimensions is possible to a limited extent; our reconstructions all have rectangular cross sections. We are investigating this issue to improve the accuracy of the reconstructed AVM. Reconstruction of vasculature requires the system to recognise blood vessel. This makes it a computer vision system and this is discussed next.

4 Reconstruction of vasculature in three dimensions

Special problems apply when reconstructing three dimensional structures from angiograms. These problems include all those mentioned in the previous section, plus others. One of these problems is the loss of the geometrical relationship between the x-ray angiograms. Its recovery is possible via a general method first developed by Longuet-Higgens (1981, 1984), and applied to angiograms by Metz and Fencil (1989), Fencil and Metz (1990), Hall (1993g). These problems are discussed in greater detail in Hall (1993c).

However, the basic difficulty to be overcome is that reconstruction is a mathematically under-determined problem. This is because reconstruction can be regarded as equivalent to recovering a matrix given its row and column sums. The reason that MRA is at an advantage over x-ray angiography for reconstruction is because it permits many more images to be acquired from different points of view. This allows reconstruction using standard methods such as filtered back projection or algebraic reconstruction methods (see Natterer 1986, Kak 1988). Reconstruction from x-ray angiograms cannot proceed that way because there are too few projections to render the approach feasible. Instead corresponding vessels in each set of cine-angiograms must be found. This requires the use of information a priori to the projections. This a priori information is used to assist correct segmentation of vessels from angiograms - the problem mentioned above. We now describe alternative knowledge representations for this information.

Many authors use descriptions of the vasculature as they appear in angiograms from specific points of view. These descriptions often appear in the form of rules in an expert system. Stansfield (1987), Suetens *et al.* (1987), Rake and Smith (1987) provide examples. Typically, these rules are of three types: low, medium, and high level. Low level rules relate to image processing methods that extract pieces of vessels as trapeziums. The medium level rules act to combine these trapeziums into strands. The high level exists to recognise strands as particular blood vessels. Notice that once they are written down rules are confined to angiograms from a particular view. A rule based approach is also taken by Delaere *et al.* (1990) so that vessels can be segmented from angiograms. A two dimensional model of vasculature is constructed for each angiogram from a specific view. Additionally, a Boolean function is used to prescribe valid structures that appear in angiograms. The Boolean function is composed from statements of the form ‘this vessel segment has a particular clinical label’, and evaluates to TRUE whenever a valid set of labels is used. Garreau *et al*. (1991) use a three-dimensional anatomical model. This frees the system from the constraint that specific points of view must be used. The model assumes that the vasculature can be regarded as a tree, which is not the case for the cerebral vasculature. This information is represented by predicates and production rules. The model takes some inter-individual topological variance into account. A particular variance may be pre-specified by a user or may be searched for using an exhaustive search technique. The system incorporates a number of heuristic rules too. These concern such things as rules for identifying the root of the tree, structural properties of the tree at furcations and a search strategy.

These existing systems are described in more detail in Hall (1993d). Their drawbacks are that they are limited to the vessels around the heart and that they have failed to reconstruct the more complicated vessel in the brain. The reason for their failure is that they do not account for all of the inter-individual variations of branching structure (*topology*) and shape, size, and position (*geometry*) that are observed amongst vasculature in the brain. Moreover, not all variations are known and this precludes constructing a reliable set of rules. We address these points by providing a knowledge representation that learns the information it requires in an incremental fashion.

Our approach is to represent a collection of vasculatures rather than a single vasculature. A three-dimensional anatomical model is built for each single vasculature and our representation combines a collection of such models in an efficient way. It is the topological variations that make up the greater part of the modelling problem and it is to this aspect of modelling that we will devote most attention. The proposed solution uses a graph as its structural base. This base is chosen not only for its generality but also because vasculature in the brain contains structures of vessels that are arranged in ring-like patterns, as in the circle of Willis (see Salamon and Huang, 197). For any individual, the nodes of a graph correspond to *vascular points*, such as furcations and end points. Graph edges correspond to *vessel segments*. Vessels as recognised in clinical texts (Salomon and Huang, 1976) are represented by paths though the graph. The topology of an individual vasculature is accounted for by the graph structure. The model is fixed in three dimensional space by labelling the nodes and edges with appropriate geometry. Edges are labelled with geometry that describes their shape, and nodes with geometry that describe such things as the relative direction of vessels.

Individual graphs in a collection are combined into a single graph that we call the *proto-graph*. Each distinct edge and each distinct node in the collection is stored exactly once in the proto-graph. The proto-graph is constructed so that any individual graph can be recovered from it as a subgraph via a Boolean valued expression that we call the *discrimination proposition*. The proto-graph is useful because it provides compact storage. More significantly the proto-graph allows a reconstruction by simultaneously matching many graphs in three dimensional space. The discrimination proposition allows the search space for reconstruction to be pruned in advance. The model learns new structural variances by adding them into the current proto-graph. This procedure yields a new proto-graph and a new discrimination proposition. A mathematical description of our model appears in Hall *et al.* (1993). We are investigating methods that will enable our system to learn vascular geometry, and statistical descriptions associated with vasculature.

Our knowledge representation has uses beside reconstruction of vasculature from biplanar angiograms. It could be used to assist reconstruction from stereo-angiograms, or to segment MRA reconstructions. It could be used as a basis for fusing x-ray images with MRA images, or even with computer tomography images. We are investigating the possible use of clinical notes that describe angiograms to reconstruct vasculature, see Hall and McKevitt (1993h). This requires the use of a natural language processor.

To assist our investigations into reconstruction we are using our model of vasculature as part of a system accurately simulated the angiographic process using a computer graphics (Hall 1994);

notice that our model of the vasculature used in the simulation has exactly the structure of the model used in reconstruction. Our simulation of the angiographic process enables us to take perspective projections from any number of directions simultaneously. The absorption of x-rays by contrast agent and their spread onto an angiographic plane are both modelled so that images of our model vessel bear good correspondence to the real world counterparts. We are able to compute rates of flow through any part of the vasculature and so the simulation of cine-angiograms is feasible. This will enable an accurate investigation into problems such as phase matching.

5 Conclusion

We have presented a range of problems that arise with the automated analysis of x-ray angiograms. Mechanisms that introduce systematic artefacts have been considered and standard solutions given. Measurement of clinically useful features has been discussed, and the problems that arise with these have been highlighted. Again, where they exist standard solutions have been referenced. Some areas of research we have deliberately ignored because they are not of immediate relevance to our own work. For example, estimating the boundary walls of the interior cavities of the heart (Duncan, 1987, Figueiredo and Leitão, 1992) and the motion of these walls (MacKay *et al.* 1982) are important areas we have omitted.

We believe that two problems have not yet been satisfactorily solved. These are phase matching of angiograms and three dimensional reconstruction. We are constructing a computer graphic model that will help us quantify the success of our reconstruction methods. For the latter problem we have proposed a unique knowledge representation that is capable of learning the information it needs from angiograms. We regard reconstruction as an example application of our model, and future work will be directed towards using it in other capacities.

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