STEREOLOGY AND MORPHOMETRY IN PATHOLOGY: AN INTRODUCTION

Yrjö Collan

Department of Pathology, University of Kuopio,
P.O.B. 6, 70211 Kuopio 21, Finland

ABSTRACT

Experimental pathology has used the methods of stereology
and morphometry and these methods have been valuable in that
context. Diagnostic histopathology can also derive advantage
from these methods. Stereology and morphometry are able to
analyse the visual patterns of the microscopic image in any
detail. Pattern recognition is an approach which usually deals
with automatic instrumentation, and aims at recognition of
patterns and features which we know are relevant for us. But
also patterns of thinking are important in the diagnostic
context. These thinking patterns lead to diagnosis. Stereology
and morphometry offer a good background for diagnostic deci-
sionmaking, and at the University of Kuopio stereology, mor-
phometry and decisionmaking are jointly studied during the
pathology course for medical students.

THE NATURE OF DIAGNOSTIC PATHOLOGY

I will start by describing an incident which occurred a
couple of days ago. I was driving my car in rain. I heard some
noise from the front but because I did not see anything spe-
cial at the moment I went on driving. Then I turned towards
left at a crossroads and when looking to the right to see
other traffic I noticed that the right windscreen wiper was no
longer there. I stopped my car about 100 meters from the
crossroads, stepped out and looked down the road I had fol-
lowed so far.

It was an early morning and the road was lonely. At first
it all looked completely normal – a scenery I could expect any
rainy morning in that place which was familiar to me. But I

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The route of my car
is shown by the arrows

I am looking
from here
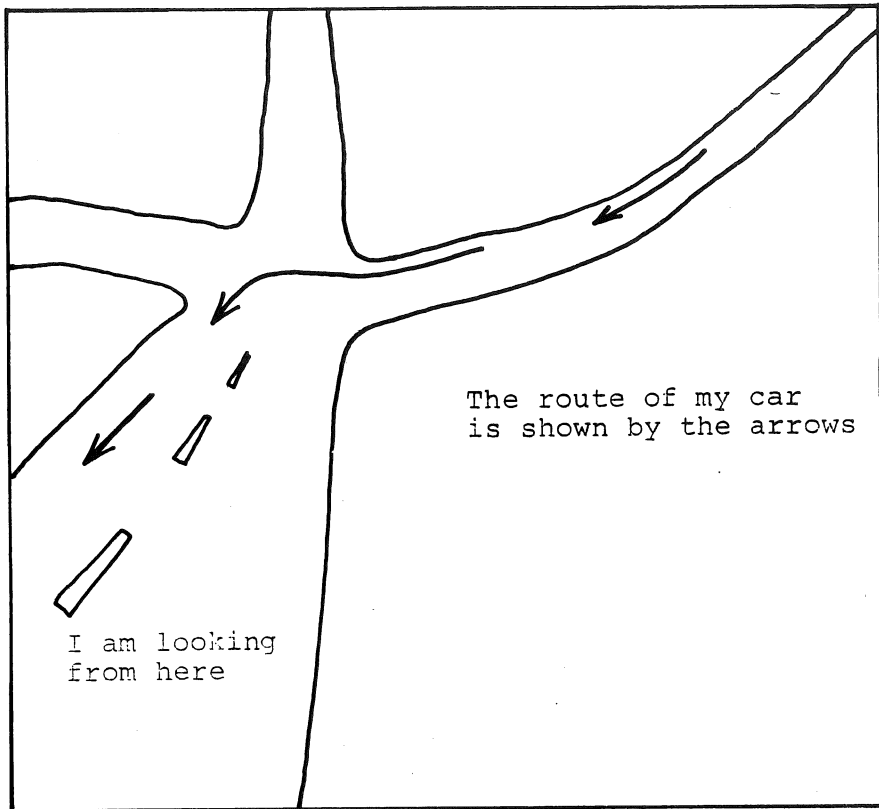
had the idea about the windscreen wiper in my mind, and be-
cause I wanted to find it I looked at the scenery a bit more
carefully. And there it was. About 300 meters away there was a
small horizontal dash in the middle of the road. I did not
know what it was but in the pattern of a road it was unusual
because the central parts of the lane are usually free from
any material. So I run to the thing and when at a distance of
about 10 meters I could definitely say it was a windscreen
wiper. And because of the context, my windscreen wiper. I took
it up, walked back to the car, fixed it and it works today as
well as ever.

     You may ask why I am speaking about windscreen wipers.
And you do it because it does not suit into the pattern you
are expecting under a title which includes pathology. But it
is your question which leads us to the answer. I talked about
windscreen wipers because the story was full of patterns and
we handle patterns in diagnostic pathology. Contextual pat-
terns, and patterns of visual images, to be exact. We have
been taught how normal tissue looks like in sections. Thereaf-
ter we have been taught how different diseases look like in
sections. In doing diagnostic work we have to decide whether
the tissue is normal or abnormal, and when abnormal what
disease entity it presents. In doing that, we detect patterns,

and see clues in these patterns which lead us to a decision
about the nature of the disease. This decision about the
nature of   disease we call diagnosis. The clues may appear
minimal and we may not even know what they represent but they
may be very helpful. It is exactly what happened to me and my
windscreen wiper. I saw something not knowing exactly what it
was, and I am a bit richer now than I was when I had lost it.

STEREOLOGY AND MORPHOMETRY

     But it has turned out that finding those faint clues and
interpreting them right is not easy and not always reproduc-
ible (Collan 1982). So physicians have turned to measurements,
which have allowed them to estimate their own performance but
in addition allowed the detection of changes which by other
means might have been left unnoticed. They have dealt with
measurements of form, morphometry. In pathology, morphometry
has mostly been applied in experimental pathology but also
diagnostic pathology has benefited in recent years. Measure-
ments on sections, however, were first made by geologists,
anatomists and histologists who tried to get an idea about 3-
dimensional structure of tissues. Because they had 3-dimensio-
nal structures in mind the methods applied were called
stereology (Underwood 1970, Weibel 1979). The principles of
geometry were and still are very important in such studies.

PATTERNS IN DIAGNOSTIC PATHOLOGY

     But before I go on I want to return to patterns. We
should realise that studying histological samples and report-
ing findings need not be dull or far from the frontlines of
science even though there may be people who feel like that.
Today we should really be interested of what we do, and how we
do our work - and also interested of this in the psychological
sense. When we dare to look at our performance, we are very
near the frontlines of scientific research of today.
     You remember the contextual patterns of the story at the
beginning of this presentation. With contextual patterns I
mean complexes like: noise in front of the car - windscreen
wiper missing - a faint dash on the rainy road, or: a patient
with enlarged liver - earlier history of melanoma - anaplastic
neoplasm in liver biopsy. Such patterns are interpreted by us
and may lead to action from our side. We think in terms on
these patterns and after thinking we decide what to do next.
In fact it has been suggested that such patterns are always
necessary in thinking and that intelligence is basicly nothing
else than recognition of various kinds of patterns. It is easy
to agree because intelligent people no doubt handle patterns
more efficiently than less intelligent people. That is my

experience anyway; simply because I call people intelligent if
they seem to handle patterns and especially contextual pat-
terns efficiently. But if the basis of intelligence is in
similar patterns on which we base our diagnostic decisions we
should realise how near the frontline of science we are work-
ing. And we should realise how basic and uniformly relevant
points in science are touched when we start to think what we
really do in diagnostic pathology. The time does not allow me
to go further but to say that the research in psychology,
human factors, safety planning, international politics, deci-
sionmaking, artificial intelligence, mathematics, automatic
data processing, and computer research are all dealing with
related problems. We see pathologists who tell us, often
slightly embarrassed, that they left research and turned to
routine pathology, as if that would mean a good bye for brain-
teasing. The truth is that they are now dealing with the side
of pathology which is very badly known, and needs intellectual
contributions to make us understand diagnostic decisionmaking
in histopathology. But patterns do not play a part in deci-
sionmaking only. In histopathology visual patterns are impor-
tant and especially such patterns intrest us today. For
handling of these patterns there are three potentially fruit-
ful approaches available. One approach deals with pattern
recognition. This approach aims at a complete description of
visual patterns and usually also at completely automatic com-
puter-aided description, so that with its help we could recog-
nize features which we have already defined. Designing of
instruments which could recognise patterns is a very important
aspect of pattern recognition. Stereology and morphometry, the
other two, do not need complicated instruments, although they
can derive benefit from them. Stereology and morphometry are
often considered identical and this may be true in some prac-
tical problems, although the definitions of these entities are
distinctly different. In histopathology we have to make a
distinction between these two because the transformation of 2-
dimensional information to 3-dimensional information may be
extremely laborious. The visual image that we analyse is 2-
dimensional. We have been happy with the information it gives
us and there is lots of evidence that histopathology has been
and still is very important in the care of sick patients. When
we measure details in the microscopic image, the results are
certainly relevant for diagnosis even without the transforma-
tion to the 3-dimensional space. If such transformation is
laborious, one would rather leave it out from the procedure
than abandon measurements altogether. One thing is certainly
true of morphometry, stereology, and patterns recognition: if
you are going to use them to make your diagnostic system
perform better you should know the principles of those
methods. You have to know what you are doing, before you can
even think of being more exact than you used to.

ARE WE AFRAID OF MEASUREMENTS ?

Principles of stereology and morphometry have been ap-
plied in experimental and basic research in histology and
histopathology. In diagnostic histopathology these methods
have not been applied to the same degree. One reason for this
is that pathologists have been afraid of losing their jobs.
True, the intuitive reaction to talks about automatic patterns
recognition, stereology or morphometry is that of suspicion.
Who is going to do all that? We pathologists or those guys
from the local Institute of Technology? There is a misunder-
standing behind this suspicion. Misunderstanding of the place
of the physician in the medical community. In the medical
community and in the diagnostic context, no automatic instru-
ments or users of those instruments can replace physicians.
Good medical background is absolutely necessary for any con-
clusions drawn for diagnostic purposes from any measurement,
be it automatic or manual. It is also understandable that
decisions leading to practical applications can be made by
physicians only. This is because a broad understanding of the
nature of disease states is necessary for such decision. On
the other hand it can be said that because measurements no
doubt are valuable, they should necessarily be applied to give
the diagnostic decision a more accurate and reproducible ba-
sis. If physicians can apply the methods the benefits are more
immediately recognised for the good of the patient. We should
not be afraid of these methods, we should rather try to find
the good they offer for the medical community.

STEREOLOGY AND MORPHOMETRY IN PATHOLOGY: THE WAY AHEAD

In fact we know quite well what these methods can offer.
They can help us find image features which might have diagnos-
tic significance and do this in an accurate and reproducible
fashion (Baak 1983). Reproducibility studies have taught us
that experience does not increase intraobserver reproducibili-
ty (Ringsted et al. 1978). It is probable that experience
helps specialists to work faster but the quality of the per-
formance (in terms of reproducibility) does not change. This
makes it quite clear that the quality of our performance
cannot be much increased with experience only – new methods
have to be applied for that purpose. Diagnostic pathology has
not had many methods for objective quality control. One has
been the follow-up of the patient. Now stereology and mor-
phometry are offering other methods for quality control. In-
terpretation of image features can now be challenged by mor-
phometric measurements, which are able to characterise the
image in any detail. Stereology and morphometry also offer a
method for testing and evaluating the limits of human perfor-
mance and the influence of human factors (Collan 1984). To sum

all this: no doubt these methods are able to lead diagnostic
histopathology from art to science. "Complete" pattern recog-
nition may also give us a new insight into the diagnostic
process and possibly even detect features which are not known
to be important today. Without education, however, the impact
of these methods will not be what it should.

EDUCATION IN STEREOLOGY AND MORPHOMETRY

     Morphometry offers us an exact way to describe the image
on which the diagnosis is based. Because we can speak in terms
of exact image features, the diagnostic system can be charac-
terised in more detail than has been possible earlier. Also
diagnostic philosophy can be based on exactly determined pa-
rameters. Understanding of these features results in decreased
dispersion on diagnostic suggestions. At least education can
be monitored by applying morphometric methods. Education can
also be made more efficient because accurate methods are
available to test alternatives.
     Diagnostic decisionmaking is central in diagnostic histo-
pathology. So, when morphometry or stereology are applied in
the diagnostic context, the decisions need be handled also.
This is why decisionmaking has an important part in the mor-
phometry training for medical students in the University of
Kuopio.
     Stereology and morphometry are introduced during the
course in pathology. The pathology course is in 3 phases:
general pathology (one term during the third year of studies),
organ pathology I (one term after general pathology), organ
pathology II (a shorter course with lectures and demonstra-
tions on gynecologic, skin, otorhinolaryngologic, pediatric
and neuropathology). During each phase 2 hours are given for
lectures and 2 hours for exercises on stereology and morpho-
metry. The study plan is as follows:

General pathology
          Lectures on geometric probability, volume fraction
          estimation, length density estimation, surface
          density estimation, numerical density estimation.

          Exercises on subjective estimation of histological
          parameters, and measurements with point and line
          grids.

Organ pathology I
          Lectures on principles of disease classifications,
          the concept of diagnosis, variation in diagnostic
          histopathology, variation in morphometric studies,
          principles of diagnostic decisionmaking.

Exercises on measurements with point and line grids, and on decision patterns.

Organ pathology II

Lectures on scientific basis of diagnostic decisions, evaluation of prognosis, basic philosophy related to the cause of death.

Exercises on decisions based on subjective evaluation of histological samples, on decisions based on morphometric analysis of histological samples, exercises on prognostic decisions, exer-cises on cause of death analysis.

What skills should the diagnostic pathologist have in stereology and morphometry? He should know the basic princi-ples outlined above and in addition he should be able to follow the developments on the field. This he has to master to avoid the unhappy situation in which pathologists could be totally dependent on technical experts whose knowledge in medical factors and associations is limited. In the next few pages the special course of this symposium tries to cover the aspects which hopefully will be able to lead the diagnostic histopathologist into the world of stereology and morphometry.

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