GROWTH MODELS FOR TOPOLOGICAL BINARY BRANCHING PATTERNS

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ABSTRACT

Binary branching patterns have been studied from a topological point of
view. The central question is how the frequency distributions of the
topologies of observed branching patterns can be understood in terms of
growth of these patterns. For this purpose techniques have been developed to
analyze the topological properties and growth models have been worked out
mathematically to calculate the expectation values for these properties. The
topologies of the branching patterns are described by the set of partitions
(degrees of subtree pairs) for all branching points in all the trees. The
model defines for each segment in a growing tree the probability of branching
which depends of the type of segment (intermediate or terminal) and of its
order (topological distance to the root). Two parameters in the model define
the strength of these dependencies. Good fits to sets of observed neuronal
dendrites could be obtained on basis of maximum likelihood criteria.

Keywords: Branching patterns, dendrites, growth models, maximum likelihood,
topology.

INTRODUCTION

Naturally grown branching patterns show variability in many if not all
of their properties. This variability is a reflection of all dynamical
aspects which occurred during the growth process. As such, questions
concerning aspects of growth may be translated into questions concerning the
variability in the structures. One property of a branching pattern is its
topology (the arrangement of its segments) and this aspect will be studied
for dendritic trees. For a binary tree of a certain degree (with a certain
number of terminal segments) there are only a finite number of different
topological arrangements. As we are dealing with 3-D branching structures
the left-right arrangement of segments in a projected image is not important.
For that reason we use the subset of topologies of binary trees whose trees
cannot be transformed into each other by exchanging the two branches at
branching points. The elements of this subset are called ambilateral types
(Fig. 1). Usually, all these arrangements will occur in naturally grown
branching patterns but the frequency of occurrence depends on the way the
patterns have grown. The link between the variability of occurrences and
modes of growth poses an intriguing problem. Three main aspects in this
problem can be distinguished.
1) the quantification of the topological properties of the trees,
2) the mathematical description of growth models and the calculation of the
expectation values for the topological properties and
3) application of the models - statistics
These aspects will be outlined in more detail in the next sections.

QUANTIFICATION OF TOPOLOGICAL PROPERTIES

A branching pattern consists of points and segments. We distinguish branching points, terminal points, intermediate segments and terminal segments. The degree of a tree is equal to its number of terminal segments and the number of branching points is equal to the degree minus one. The distribution of the degree of all trees may thus be indicative for the 'age' of the sample. All branching patterns can be arranged into a well-ordered scheme on basis of their ambilateral type (Van Pelt and Verwer, 1983) as shown in Fig. 1 for trees of degree 6.
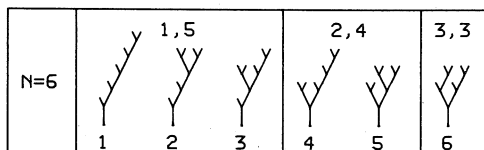

Fig. 1. Ambilateral types of degree n=6 (number of terminal segments). The numbers in pairs denote the degrees of the first-order subtrees.

The first step in the topological analysis of a set of observed trees is to take together all trees of the same degree and build frequency distributions of their ambilateral types. These distributions may be subsequently tested against model predictions. A major drawback of this approach is that the number of ambilateral types per degree (and thus the number of classes in the distribution) very rapidly increases with the degree. For instance, there are already 2179 ambilateral types of degree 14.

Another representation of the topological properties of the trees is based on partitions. Each branching point in a tree gives rise to two subtrees and as such the degree of a tree is partitioned at its first bifurcation point over the two subtrees (Fig. 2). For instance, there are
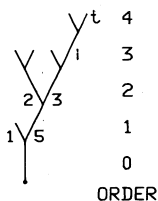

Fig. 2. Ambilateral type of degree 6. The figure shows an intermediate segment (i), a terminal segment (t) and the two non-trivial partitions (1,5) and (2,3). Each segment is labelled by an order number indicating its topological distance to the root. The root itself has order zero.

three ways to partition degree 6, i.e. (1,5), (2,4) and (3,3). A tree can be decomposed into all its partitions and the topology of the tree is completely defined by this set of partitions if the tree can be reconstructed unambiguously from this set. If there are more partitions of the same degree in the tree, this is, however, not possible. For instance, both 9(4(1 3)5(1 4(2 2))) and 9(4(2 2)5(1 4(1 3))) can be reconstructed from the set {(1,3),(2,2),(1,4),(4,5)}. Thus, by the decomposition, the exact location of some partitions in the tree is lost but the frequency of occurrence of the partitions is scored. For the stochastic growth models it appears that only these partition frequencies are important so that one can conclude that within the context of these growth models no topological information is lost by this decomposition. Following this approach, the same can be done for all trees in a sample and the result is an array of partition frequencies. If the largest tree is of degree 14 then the decomposition gives rise to partitions of degree 14 and of lower degree. There are maximal 47 different partitions of degree 14 and lower, i.e. (1,3), (2,2), (1,4), ... etc, excluding the trivial partitions (1,1) and (1,2). We observe thus

an enormous data reduction from 2179 possible topological types into 47 possible partitions (Van Pelt and Verwer, 1984). The 'degree distribution' as indicative for the 'age' of the complete trees, however, is lost by this decomposition.

MATHEMATICAL DESCRIPTION OF GROWTH MODELS – FORMULAE FOR THE PARTITION PROBABILITIES

The growth of branching patterns will be described as a series of branching events while in each event only one segment branches. The growth model defines for each segment in a growing tree the probability of branching and all branching probabilities are normalized per tree. Each branching event in a tree is thus the realization of a stochastic process defined on all segments in that tree. After n-1 branching events the tree will be of degree n (if the process was started with one segment) and its ambilateral type can be determined. Many trees may have grown in this way resulting in a frequency distibution of all ambilateral types of degree n. The following growth rules have been studied. The branching probability of a segment depends of its type i.e. a terminal or intermediate segment and of its order (Fig. 2), i.e. the topological distance to the root. The strength of these dependencies is determined by two parameters R and S. The branching probabilities pt of a terminal segment and pi of an intermediate segment are now defined as

$$pt = \frac{1}{C} 2^{-S\gamma} \quad \text{and} \quad pi = \frac{1}{C} R\, 2^{-S\gamma}. \tag{1}$$

The variable γ denotes the order of the segment. The parameter S denotes the strength of the order dependency and may have any real value. The parameter R defines the ratio of branching probabilities of intermediate and terminal segments of equal order, R = pi/pt. For convenience, we also use the parameter Q = R/(R+1) = pi/(pi+pt). The constant C is a normalization constant such that the branching probabilities of all n terminal segments and n-1 intermediate segments in a tree of degree n sum to one. The growth rules have been formulated such that any subtree in a tree will develop on subsequent branching as if it was a complete tree. Thus, the topological properties of the trees and of all the subtrees will have the same statistical distributions. For instance, this is valid for the partitions of all branching points in the tree. As a consequence the partitions in a tree are independent from each other and the probability of the complete tree within its set will be the product of the probabilities of all its actual partitions (only corrected with a factor 2 for each occurrence of equal-degree, unequal-type subtree pairs). For the elaboration of the growth model it suffices to calculate only the partition probabilities. These calculations have been done for the general case of arbitrary values of the parameters Q and S but also in some special cases for particular values of these parameters. In the general case, however, it was not possible to derive analytical expressions for the partition probabilities as it was in the special cases. These cases will now be described in more detail and expressions are given for the partition probabilities p(r,n-r;Q,S) where (r,n-r) denotes the partition (of degree n) and Q and S the parameter values.
A) S=0. There is no order dependency for S=0 and all segments of the same type have the same branching probability (Van Pelt and Verwer, 1983, 1985).
A1) Q=0 (R=0). Intermediate segments are not allowed to branch and we have only branching of terminal segment. This particular model is called terminal growth.

$$p(r,n-r;0,0) = 2^{1-\delta(r,n-r)}/(n-1) \quad . \tag{2}$$

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The Kronecker delta $\delta(x,y)$ equals one if x=y and equals zero if x≠y. The probabilities p(1,4;0,0) and p(2,3;0,0) are indicated by a diamond in Fig. 3. An expression for the ambilateral type probabilities for this growth model was already derived by Harding (1971).

A2) Q=0.5 (R=1). For Q=0.5 we have equal branching probabilities for intermediate and terminal segments and herewith for all segments in the tree. This particular model is called segmental growth.

$$p(r,n-r;0.5,0) = 2^{1-\delta(r,n-r)} N_\tau^r N_\tau^{n-r} / N_\tau^n \quad , \quad \text{while} \quad N_\tau^n = \binom{2n-1}{n}/(2n-1) \quad . \quad (3)$$

The probabilities p(1,4;0.5,0) and p(2,3;0.5,0) are indicated by a square in Fig. 3.

A3) Q≠0 and Q≠0.5. Under these conditions both intermediate and terminal segments are allowed to branch with unequal branching probabilities.

$$p(r,n-r;Q,0) = 2^{1-\delta(r,n-r)} \cdot \{1+Q(\frac{n(n-1)}{2r(n-r)} - 2)\} \cdot \frac{1}{n-1-Q} \cdot \prod_{i=1}^{r-1} \frac{1-Q/i}{1-Q/(i+n-r-1)} \quad . \quad (4)$$

The probabilities p(1,4;Q,0) and p(2,3;Q,0) are given by the dotted lines in the midplanes in Fig.3. They show that the (1,4)-partition probability increases for increasing values of R and will reach the value one for large R. The (2,3)-partition probability behaves opposite. For large R the partitions thus are very asymmetrical. For R=0, however, both the (1,4) and the (2,3) probability still have finite values and the partitions will not be completely symmetrical. Dacey and Krumbein (1976) have calculated the ambilateral type probabilities for the parameter values R=0, R=1 and R=2 by enumerating all possible growth paths.

B) S≠0. For non-zero values of S the branching probability of a segment depends of its position in the tree. The branching probability increases with order for negative values of S and decreases with order for positive values of S (Van Pelt and Verwer, submitted). The (1,4)- and (2,3)-partition probabilities are shown in Fig. 3 for a finite part of the parameter space.
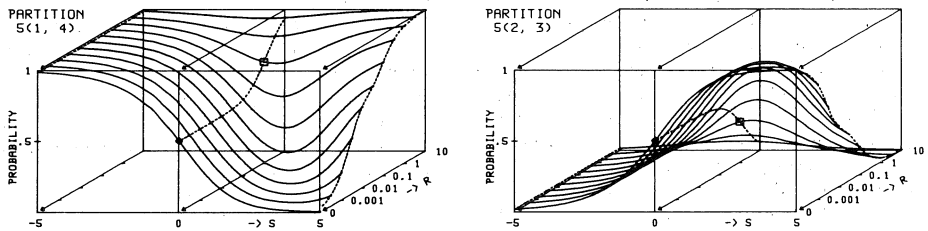

Figure 3. Probabilities of the partitions 5(1,4) and 5(1,3) plotted for the parameter domain -5≤S≤5 and 0≤R≤10. The dotted curves in the midplanes show the probabilities if there is no order-dependency in the branching probabilities. Terminal and segmental growth are indicated by a diamond and a square, respectively.

It appears that the asymmetrical (1,4) partition for positive values of S has smaller probability than in the midplane while the more symmetrical (2,3)-partition probability goes up and reaches the value one for R=0 and large values of S. This general model thus succeeds in predicting both complete asymmetrical and complete symmetrical trees.

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APPLICATION OF THE MODELS - STATISTICS

     Roughly two ways can be distinguished in the application of the models
to observations.
1) A particular mode of growth is hypothesized and a statistical test is
performed to the data. The observed branching patterns are converted to
their partition frequency distributions and each distribution (of a
particular degree) is tested against the model distribution by means of a
Chi-square test or a Kolmogorov goodness-of-fit test for discrete
distributions (Conover, 1972). The outcomes of all the tests may be combined
by means of Fisher's test to get an overall level of significance for the
hypothesis (Koziol and Perlman, 1978). An alternative procedure consists of
the construction of a new distribution and criteria to assign unambiguously
all partitions (of any degree) to its classes. A model distribution has to
be constructed in a similar way. Subsequent testing then yields one test
outcome for the whole sample (Uylings et al., 1983; Verwer and Van Pelt,
1983; Van Pelt and Verwer, 1984).
2) An optimal fit of the model to the sample of partitions is searched. This
search tries to find those values of the parameters for which the sample is
predicted by the model with maximum likelihood. This optimum may be found
analytically for the S=0 model, but for S≠0 it can only be found by
calculating the likelihood on a grid in (R,S)-space, searching the maximum
and eventually following with a subsequent search on a finer grid. An
example of the shape of the log-likelihood plane is given in Fig. 4.
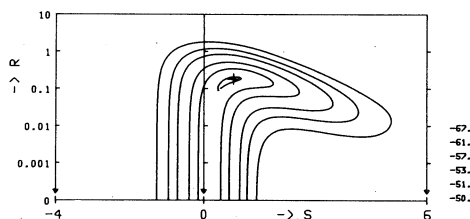

Fig. 4. Contours of equal likelihood for the set of partitions,
originated from a sample of multipolar non-pyramidal cells. These cells
were kindly provided by Dr H.B.M. Uylings of our institute. The
partition frequencies $N(i,j)$ in this set are $N(1,3)=18$, $N(2,2)=9$,
$N(1,4)=5$, $N(2,3)=10$, $N(1,5)=4$, $N(2,4)=3$, $N(3,3)=2$, $N(1,6)=1$, $N(2,5)=2$,
$N(3,4)=3$, $N(1,7)=2$, $N(2,6)=1$, $N(3,5)=1$, $N(4,6)=1$. The maximum
log-likelihood value of -49.9 occurs at the position S=0.8 and R=0.18
(Q=0.15) which is indicated by the cross. The log-likelihood values of
the contours are given at the right side of the figure. Without
order-dependency, the parameter space reduces to the mid-axis at S=0. A
maximum likelihood search on this axis would have resulted in a
log-likelihood value of -50.3 at R=0.

Characteristic for the shape is the ridge which runs parallel to the R-axis
for increasing R and small values of S, turns towards the positive
S-direction and bends slowly back to smaller values of R, hereby decreasing
in amplitude if the maximum is passed. The part of the ridge parallel to the
R-axis indicates that here the likelihood is rather insensitive for
variations in parameter R. The quality of the fit, however, is not deducible
from the likelihood value itself. For that purpose we applied the Kolmogorov
goodness-of-fit test for the best-fit parameter set and the results are given
in Table 1. The application of Fisher's test to all these significance
levels yields an overall level of significance of 0.94 indicating that the
quality of the fit is very good.

                                                             11.25

Table 1. The levels of significance obtained by the Kolmogorov goodness-of-fit test for discrete distributions of the model $(Q;S)=(0.15;0.8)$ against the data shown in Fig. 4.   Distributions with less than 5 observations (degree 8 and 10) are not included.

degree of partition	number of observations	level of significance
4	27	0.70
5	15	0.45
6	9	0.93
7	6	0.84

Fisher's test : 0.94

Although the attained levels of significance are conservative because the parameter set was deduced from the same data they give an indication of the quality of the fit especially in comparison with outcomes from other models. The Chi-square procedure may also be used for the best-fit search but restrictions are then imposed on the number of observations per class (Verwer et al., submitted).

ACKNOWLEDGEMENTS

REFERENCES

Conover WJ. A kolmogorov goodness-of-fit test for discontinuous
      distributions. J Am Statist Ass 1972; 67: 591-596.
Dacey MF, Krumbein WC. Three growth models for stream channel networks.
      J Geol 1976; 84: 153-163.
Harding EF. The probabilities of rooted tree-shapes generated by
      random bifurcation. J Appl Prob 1971; 3: 44-77.
Koziol JA, Perlman MD. Combining independent chi-squared tests.
      J Am Statist Ass 1978; 73: 753-763.
Uylings HBM, Verwer RWH, Van Pelt J, Parnavelas JG. Topological analysis
      of dendritic growth at various stages of cerebral development.
      Acta Stereol 1983; 2: 55-62.
Van Pelt J, Verwer RWH. The exact probabilities of branching patterns
      under terminal and segmental growth hypotheses.
      Bull Math Biol 1983; 45: 269-285.
Van Pelt J, Verwer RWH. New classification methods of branching patterns.
      J Microsc 1984; 136: 23-34.
Van Pelt J, Verwer RWH. Growth models (including terminal and segmental
      branching) for topological binary trees.
      Bull Math Biol 1985; 47: 323-336.
Van Pelt J, Verwer RWH. Topological properties of binary trees grown with
      order-dependent branching probabilities. Bull Math Biol, submitted.
Verwer RWH, Van Pelt J. A new method for the topological analysis
      of neuronal tree structures. J Neurosci Meth 1983; 8: 335-351.
Verwer RWH, Van Pelt J, Noest AJ. Estimation of parameters in topological
      growth models for neuronal trees. J Neurosci Meth (submitted).