Asymmetry tests for Bifurcating Auto-Regressive Processes with missing data

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Abstract

We present symmetry tests for bifurcating autoregressive processes (BAR) when some data are missing. BAR processes typically model cell division data. Each cell can be of one of two types odd or even. The goal of this paper is to study the possible asymmetry between odd and even cells in a single observed lineage. We first derive asymmetry tests for the lineage itself, modeled by a two-type Galton-Watson process, and then derive tests for the observed BAR process. We present applications on both simulated and real data.

Keywords: Bifurcating autoregressive processes, Cell division data, Missing data, Two-type Galton-Watson model, Wald’s test.

2000 MSC: 62M07, 62F05, 60J80, 62P10

1. Introduction

Bifurcating autoregressive processes (BAR) were first introduced by Cowan and Staudte [1986]. They generalize autoregressive processes when data are structured as a binary tree. Typically, they are involved in statistical studies of cell lineages, since each cell in one generation gives birth to two offspring in the next one. These two offspring sometimes need to be distinguished according to some biological property, leading to the notion of type. Cell lineage data consist of observations of some quantitative characteristic of the cells (e.g. their growth rate) over several generations descended from an initial cell. More precisely, the initial cell is labelled 1, and the two offspring of cell \( k \) are labelled \( 2k \) and \( 2k + 1 \), where \( 2k \) stands for one type, thus called even, and \( 2k + 1 \) for the other type, thus called odd. If \( X_k \) denotes the quantitative characteristic of cell \( k \), then the first-order asymmetric BAR process is given by

\[
\begin{align*}
X_{2k} &= a + bX_k + \varepsilon_{2k}, \\
X_{2k+1} &= c + dX_k + \varepsilon_{2k+1},
\end{align*}
\]

for all \( k \geq 1 \). The noise sequence \((\varepsilon_{2k}, \varepsilon_{2k+1})\) represents environmental effects, while \( a, b, c, d \) are unknown real parameters related to the inherited effects. They are allowed to be different for the odd and even sisters.

Various estimators are studied in the literature for the unknown parameters \( a, b, c, d \), see [Bercu et al., 2009, Delmas and Marsalle, 2010, Guyon, 2007]. This paper derives further properties of the estimators given in [de Saporta et al., 2011], where the genealogy is modeled by a two-type Galton Watson process (GW), allowing the reproduction laws to depend on both the mother’s and daughter’s types. Indeed, the aim of this paper is to propose asymmetry tests for both the two-type GW process defining the genealogy of the cells, as well as the BAR process with missing data.
More precisely, we first study the difference of the means of the reproduction laws for even and odd mother cells in the GW process. Then we investigate the difference of the parameters \( a, b, c, d \) and the difference between the fixed points \( a/(1-b) \) and \( c/(1-d) \). We propose Wald’s type tests based on the asymptotic normality of the various estimators. A detailed study on simulated data, as well as a new investigation of the *Escherichia coli* data of [Stewart et al. 2005](#) are provided.

The paper is organized as follows. We start with introducing in Section 2 some notation that will be used throughout the paper. In Section 3 we derive Wald’s tests for the two-type GW process describing the genealogy of the cells. In Section 4 we derive Wald’s test for the BAR process, to test asymmetry of its parameters. In section 5 we apply our tests to simulated data. Finally, in Section 6 we apply our tests to [Stewart et al. 2005](#) data.

2. Notation

For all \( n \geq 1 \), denote the n-th generation by \( G_n = \{ k \in \mathbb{N} | 2^n \leq k \leq 2^{n+1} - 1 \} \). Denote by \( T_n = \bigcup_{i=0}^{p} G_i \) the sub-tree of all cells up to the n-th generation. The cardinality \( |G_n| \) of \( G_n \) is \( 2^n \), while that of \( T_n \) is \( |T_n| = 2^{n+1} - 1 \). We need to distinguish the cells in \( G_n \) and \( T_n \) according to their type. The type even will be labelled type 0 and the type odd will be labelled type 1. We set \( G_0^0 = G_0 \cap (2\mathbb{N}), G_1^0 = G_1 \cap (2\mathbb{N} + 1), T_0^0 = T_0 \cap (2\mathbb{N}), T_1^0 = T_1 \cap (2\mathbb{N} + 1) \). We encode the presence or absence of the cells by the process \( (\delta_i) \): if cell \( k \) is observed, then \( \delta_k = 1 \), if cell \( k \) is missing, \( \delta_k = 0 \).

We define the sets of observed cells as \( G_n^0 = \{ k \in G_n : \delta_k = 1 \} \) and \( T_n^0 = \{ k \in T_n : \delta_k = 1 \} \). Finally, let \( \mathcal{E} \) be the event corresponding to the cases when there are no cell left to observe in the current generation: \( \mathcal{E} = \bigcup_{i \geq 1} \{ |G_i^0| = 0 \} \) and \( \overline{\mathcal{E}} \) the complementary set of \( \mathcal{E} \). For \( n \geq 1 \), we define the number of observed cells among the n-th generation, distinguishing according to their type: \( Z_n^0 = |G_n^0 \cap 2\mathbb{N}|, Z_n^1 = |G_n^1 \cap (2\mathbb{N} + 1)| \), and we set, for all \( n \geq 1 \), \( Z_n = (Z_n^0, Z_n^1) \). Note that for \( i \in \{ 0, 1 \} \) and \( n \geq 1 \) one has \( Z_n^i = \sum_{k \in G_n^{i}} \delta_{2k+i} \).

3. Asymmetry in the lineage

We now describe the mechanism generating the observation process \( (\delta_i) \). The resulting process \((Z_n)\) is a two-type GW process. We recall some assumptions similar to [de Saporta et al. 2011](#) and mostly taken from [Harris 1963](#).

3.1. Model and assumptions

We define the cells genealogy by a two-type GW process \((Z_n)\). All cells reproduce independently and with a reproduction law depending only on their type. For a mother cell of type \( i \in \{ 0, 1 \} \), we denote by \( p^{(i)}(j_0, j_1) \) the probability that it has \( j_0 \) daughter of type 0 and \( j_1 \) daughter of type 1. For the cell division process we are interested in, one clearly has \( p^{(0)}(0,0) + p^{(0)}(1,0) + p^{(0)}(0,1) + p^{(0)}(1,1) = 1 \). The reproduction laws have moments of all order, and we can thus define the descendants matrix \( \mathbf{P} \)

\[
\mathbf{P} = \begin{pmatrix}
p_{00} & p_{01} \\
p_{10} & p_{11}
\end{pmatrix},
\]

where \( p_0 = p^{(0)}(1,0) + p^{(0)}(1,1) \) and \( p_1 = p^{(0)}(0,1) + p^{(0)}(1,1) \), for \( i \in \{ 0, 1 \} \); \( p_{ij} \) is the expected number of descendants of type \( j \) of a cell of type \( i \). It is well-known that when all the entries of the matrix \( \mathbf{P} \) are positive, \( \mathbf{P} \) has a strictly dominant positive eigenvalue, denoted \( \pi \), which is also simple. We make the following main assumption.

**Remark** All entries of the matrix \( \mathbf{P} \) are positive and the dominant eigenvalue is greater than one: \( \pi > 1 \).

In this case, there exist left and right eigenvectors for \( \pi \) which are component-wise positive. Let \( z = (z^0, z^1) \) be such a left eigenvector satisfying \( z^0 + z^1 = 1 \). This dominant eigenvalue \( \pi \) is related to the extinction of the process: assumption **(AO)** means that the GW process \((Z_n)\) is super-critical, and ensures that extinction is not almost sure: \( \mathbb{P}(\mathcal{E}) < 1 \). Besides, on \( \overline{\mathcal{E}} \), \( |T_n|^{-1} \sum_{i=1}^{n} Z_i^1 \) converges to \( z^1 \), meaning that \( z^1 \) is the asymptotic proportion of cells of type \( i \) in a given sub-tree.

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3.2. Asymmetry test

We first propose estimators for the parameters of the GW process and study their asymptotic properties. Our context is very specific because the available information given by $(\delta_t)$ is more precise than the one given by $(Z_t)$ usually used in the literature, see e.g. [Guttorp, 1991]. The empirical estimators of the reproduction probabilities using data up to the $n$-th generation are then, for $i, j_0, j_1 \in [0, 1]$

$$\hat{p}^{(i)}_n(j_0, j_1) = \frac{\sum_{k \leq T_{n-1}} \delta_{2k+i} \phi_{j_0}(\delta_{2k+i}) \phi_{j_1}(\delta_{2k+i+1})}{\sum_{k \leq T_{n-1}} \delta_{2k+i}},$$

where $\phi_0(x) = 1 - x$, $\phi_1(x) = x$, and if the denominators are non zero (the estimation is zero otherwise). The strong consistency is easily obtained on the non-extinction set $\bar{E}$ e.g. by martingales methods as in [de Saporta et al., 2011].

**Lemma 3.1.** Under (AO) and for all $i, j_0$ and $j_1$ in $[0, 1]$, one has $\lim_{n \to \infty} \mathbb{P} \{ |\hat{p}^{(i)}_n(j_0, j_1) - p^{(i)}(j_0, j_1) | \} = 0$ a.s.

Set $p^{(i)} = (p^{(0)}(0, 0), p^{(0)}(1, 0), p^{(1)}(0, 1), p^{(1)}(1, 1))^t$ the vector of the 4 reproduction probabilities for a mother of type $i$, $p = ((p^{(0)})^t, (p^{(1)})^t)$ the vector of all 8 reproductions probabilities and $\hat{p}_n = (\hat{p}^{(0)}_n(0, 0), \ldots, \hat{p}^{(1)}_n(1, 1))^t$ its estimator. As $P(\bar{E}) \neq 0$, we define the conditional probability $P_{\bar{E}}$ by $P_{\bar{E}}(A) = P(A \cap \bar{E})/P(\bar{E})$ for all event $A$.

**Theorem 3.2.** Under assumption (AO), we have the convergence $\sqrt{\text{Var}_{n-1}}(\hat{p}_n - p) \xrightarrow{L} N(0, V)$ on $(\bar{E}, P_{\bar{E}})$, with

$$V = \left( \begin{array}{cc} V_0/z^0 & 0 \\ 0 & V^1/z^1 \end{array} \right)$$

and for all $i \in [0, 1]$, $V^i = W^i - p^{(i)}(p^{(i)})^t$, $W^i$ is a 4x4 matrix with the entries of $p^{(i)}$ on the diagonal and 0 elsewhere.

**Proof:** For all $n \geq 2$, and $q \geq 1$, set

$$M^{(n)}_q = \frac{1}{\sqrt{\text{Var}_{n-1}}} \sum_{k \leq T_{n-1}} q \begin{pmatrix} \delta_{2k+1}(1 - \delta_{2k+2})(1 - \delta_{2k+3}) - p^{(0)}(0, 0) \\ \delta_{2k}(1 - \delta_{2k+1}) - p^{(0)}(1, 0) \\ \delta_{2k+1}(1 - \delta_{2k+2}) - p^{(0)}(0, 1) \\ \delta_{2k+2}(1 - \delta_{2k+3}) - p^{(1)}(0, 0) \\ \delta_{2k+1}(1 - \delta_{2k+2}) - p^{(1)}(1, 0) \\ \delta_{2k+2}(1 - \delta_{2k+3}) - p^{(1)}(0, 1) \end{pmatrix}.$$

Let $(\mathcal{G}_q)$ be the filtration of cousins cells: $\mathcal{G}_0 = \sigma(\delta_1, \delta_2, \delta_3)$ and for all $q \geq 1$, $\mathcal{G}_q = \mathcal{G}_{q-1} \vee \sigma(\delta_{2q}, \delta_{4q+1}, \delta_{4q+2}, \delta_{4q+3})$. For all $n \geq 2$, $(M^{(n)}_q)$ is a $(\mathcal{G}_q)$-martingale with finite moments of all order. We apply Theorem 3.II.10 of [Duflo, 1997] to this sequence of martingales and with the stopping times $n_p = \tau_{n-2}$. The $P_{\bar{E}}$ a.s. limit of the increasing process is

$$\frac{1}{\text{Var}_{n-1}} \sum_{k \leq T_{n-1}} \frac{\delta_{2k} V^0}{\text{Var}_{n-1}} \frac{\delta_{2k+1} V^1}{\text{Var}_{n-1}} \xrightarrow{P_{\bar{E}}} G = \begin{pmatrix} z^0 V^0 & 0 \\ 0 & z^1 V^1 \end{pmatrix}.$$

In addition, the Lindeberg condition holds as the $\delta_k$ have finite moments of all order. Thus, we obtain the convergence $M^{(n)}_{\tau_{n-2}} \xrightarrow{L} N(0, G)$ on $(\bar{E}, P_{\bar{E}})$. On the other hand, $\Lambda^{-1}_n (\tau_{n-1} \text{Var}_{n-1}^{-1} M^{(n)}_{\tau_{n-2}}) = \sqrt{\text{Var}_{n-1}} (\hat{p}_n - p)$, with

$$\Lambda_n = \begin{pmatrix} \sum_{k=1}^n Z_k^1 I_4 \\ 0 \end{pmatrix}.$$

and $I_4$ is the identity matrix of size 4. As $\tau_{n-1}^{-1} \sum_{k=1}^n Z_k$ converges almost surely to $z^i$ on $(\bar{E}, P_{\bar{E}})$, we have the asymptotic normality as announced, using Slutsky’s lemma.

Using the asymptotic normality of the $\hat{p}^{(i)}_n(j_0, j_1)$, we can derive Wald’s test for the asymmetry of the means of the reproduction laws. Set $m = (p^{(0)}(1, 0) + p^{(0)}(0, 1) + 2p^{(1)}(1, 1)) - (p^{(1)}(1, 0) + p^{(1)}(0, 1) + 2p^{(1)}(1, 1))$ the difference of
the means of the types 0 and 1 reproduction laws and \( \hat{\mu}_n = (\hat{\mu}_n(0,1) + \hat{\mu}_n(0,1) + 2\hat{\mu}_n(1,1)) \) its empirical estimator. Set \( \mathbf{H}_{0}^{GW} = m = 0 \) the symmetry hypothesis and \( \mathbf{H}_{1}^{GW} = m \neq 0 \). Let \( Y_n^{GW} \) be the test statistic defined by \( Y_n^{GW} = \frac{\Delta_n^{GW}}{\sqrt{\sum_{i=1}^{n} Z_i}} \).\( \Delta_n^{GW} = \sum_{i=1}^{n} \sum_{j=1}^{n} Y_{ij} \) is the empirical version of \( V \), where \( z^j \) is replaced by \( \sum_{i=1}^{n} Z_i \) and the \( p^{(0)}(j_0, j_1) \) are replaced by \( \hat{\mu}_n(j_0, j_1) \) via Lemma 3.1. \( \hat{\mu}_n \) converges a.s. to \( \mu \) and the test statistic has the following asymptotic properties.

**Theorem 3.3.** Under assumption \((\text{AO})\) and the null hypothesis \( \mathbf{H}_{0}^{GW} \), one has \( (Y_n^{GW})^2 \xrightarrow{L} \chi^2(1) \) on \((\mathbb{E}, \mathbb{P}_E)\); and under the alternative hypothesis \( \mathbf{H}_{1}^{GW} \), one has \( \lim_{n \to \infty} (Y_n^{GW})^2 = +\infty \) a.s. on \((\mathbb{E}, \mathbb{P}_E)\).

**Proof:** Let \( g \) be the function defined from \( \mathbb{R}^3 \) onto \( \mathbb{R} \) by \( g(x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8) = (x_2 + x_3 + 2x_4) - (x_5 + x_7 + 2x_8) \), so that \( \hat{m}_n - m = g(\hat{\mu}_n) - g(p) \), and \( \delta \Sigma \) is the gradient of \( g \). Thus, Theorem 3.2 yields \( \sqrt{|\Delta_n|} \sum_{i=1}^{n} (g(\hat{\mu}_n) - g(p)) \xrightarrow{L} \mathcal{N}(0, \Delta_n^{GW}) \) on \((\mathbb{E}, \mathbb{P}_E)\), with \( \Delta_n^{GW} = \sum_{i=1}^{n} \sum_{j=1}^{n} Y_{ij} \). Under the null hypothesis \( \mathbf{H}_{0}^{GW} \), \( g(p) = m \), so that \( \lim_{n \to \infty} \frac{\Delta_n^{GW}}{\sqrt{\sum_{i=1}^{n} Z_i}} \xrightarrow{L} \chi^2(1) \) on \((\mathbb{E}, \mathbb{P}_E)\). One then uses Slutsky’s lemma to replace \( \Delta_n^{GW} \) by its estimator \( \hat{\Delta}_n^{GW} \) and obtain the first convergence. Under the alternative hypothesis \( \mathbf{H}_{1}^{GW} \), since \( Y_n^{GW} = \frac{\Delta_n^{GW}}{\sqrt{\sum_{i=1}^{n} Z_i}} \), and \( \hat{\mu}_n \) converges to \( m \neq 0 \), \( Y_n^{GW} \) tends to infinity a.s. on \((\mathbb{E}, \mathbb{P}_E)\). \( \square \)

4. Asymmetry in cells characteristic

We now turn to the study of asymmetry of the BAR model with missing data. We first recall some asymptotic results on the estimation of the BAR parameters proved in (de Saporta et al., 2011).

4.1. Model and assumptions

We consider the first-order asymmetric BAR process given by Eq. (1). We assume that \( \mu_X^1[X] < \infty \). Moreover the parameters satisfy 0 < max(|\( b_i |, |d_i |) < 1 \). Denote by \( F = (F_n) \) the natural filtration associated with the BAR process: \( F_n = \sigma(X_k \in \mathbb{N}) \). In all the sequel, we shall make use of the following moment and independence hypotheses.

**(AN.1)** For all \( n \geq 0 \) and for all \( k \in \mathbb{N} + 1 \), \( \epsilon_k \) belongs to \( L^2 \) with \( \sup_{n \geq 0} \sup_{k \in \mathbb{N} + 1} \mathbb{E}[\epsilon_k^2 | F_n] < \infty \) a.s. Moreover, there exist \( \sigma^2 > 0 \) and \( \rho \) such that \( \forall n \geq 0 \) and \( k \in \mathbb{N} + 1 \), \( \mathbb{E}[\epsilon_k^2 | F_n] = 0 \) and \( \mathbb{E}[\epsilon_k^2 | F_n] = \sigma^2 \) a.s.; \( \forall n \geq 0 \), \( \forall k \neq l \in \mathbb{N} + 1 \), with \( [k/2] = [l/2] \), \( \mathbb{E}[\epsilon_k \epsilon_l | F_n] = \rho \) a.s., where \( [x] \) denotes the largest integer less then or equal to \( x \).

**(AN.2)** For all \( n \geq 0 \) the random vectors \( (\epsilon_{2k}, \epsilon_{2k+1}) \), \( k \in \mathbb{N} + 1 \) are conditionally independent given \( F_n \).

**(A1)** The sequence \( (\delta_k) \) is independent from the sequences \( (X_k) \) and \( (\epsilon_k) \).

The least-squares estimator of \( \theta = (a, b, c, d) \) is given for all \( n \geq 1 \) by \( \hat{\theta}_n = (\hat{a}_n, \hat{b}_n, \hat{c}_n, \hat{d}_n) \) with

\[
\hat{\theta}_n = \sum_{k \in \mathbb{N} + 1} \left( \begin{array}{c}
\delta_{2k} X_{2k} \\
\delta_{2k} X_{2k} \\
\delta_{2k+1} X_{2k+1} \\
\delta_{2k+1} X_{2k+1}
\end{array} \right), \quad \sum_n = \sqrt{n} \left( \begin{array}{c}
S_n^0 \\
S_n^1 \\
S_n^0 \\
S_n^1
\end{array} \right), \quad S_n^0 = \sum_{k \in \mathbb{N} + 1} \delta_{2k} X_{2k} \begin{pmatrix} X_k \\
X_k
\end{pmatrix}, \quad S_n^0 = \sum_{k \in \mathbb{N} + 1} \delta_{2k+1} X_{2k+1} \begin{pmatrix} 1 \\
X_k \\
X_k
\end{pmatrix}.
\]

Denote also \( L^0, L^1, L^{0,1} \) the a.s. limits: \( \lim_{n \to \infty} \frac{\sum_{j=1}^{n} S_n^0 |T_n^*|}{\sqrt{\sum_{j=1}^{n} T_n^*}} = \mathbb{P}[L^0], \quad \lim_{n \to \infty} \frac{\sum_{j=1}^{n} S_n^{0,1} |T_n^*|}{\sqrt{\sum_{j=1}^{n} T_n^*}} = \mathbb{P}[L^{0,1}] \) (see Proposition 4.2 of (de Saporta et al., 2011)). We now recall Theorems 3.2 and 3.4 of (de Saporta et al., 2011).

**Theorem 4.1.** Under (AN.1-2), (AO) and (A1), the estimator \( \hat{\theta}_n \) is strongly consistent \( \lim_{n \to \infty} \frac{\hat{\theta}_n}{|L^0|} = \mathbb{P}[\theta] \) a.s.

In addition, we have the asymptotic normality \( \sqrt{|T_n^*|} (\hat{\theta}_n - \theta) \xrightarrow{L} \mathcal{N}(0, \Sigma \Gamma \Sigma^{-1}) \) on \((\mathbb{E}, \mathbb{P}_E)\), where

\[
\Sigma = \begin{pmatrix}
L^0 & 0 \\
0 & L^1
\end{pmatrix}, \quad \Gamma = \begin{pmatrix}
\sigma^2 L^{0,1} & \rho L^{0,1} \\
\rho L^{0,1} & \sigma^2 L^1
\end{pmatrix},
\]
4.2. Asymmetry tests

Using Theorem 4.2, we now propose two different asymmetry tests. The first one compares the couples \((a, b)\) and \((c, d)\). Set \(H_0^2\): \((a, b) = (c, d)\) the symmetry hypothesis and \(H_1^2\): \((a, b) \neq (c, d)\). Let \((Y_n^f)\) be the test statistic defined by 
\[
Y_n^f = |T_n|^1/2(\hat{\Delta}_n)^{-1/2}(\hat{a}_n - \hat{b}_n - \hat{d}_n)^T, \quad \text{with} \quad \hat{\Delta}_n = \text{dgc}[T_n^{-1}\Sigma_n^{-1}T_n^{-1}\Sigma_n^{-1}].
\]

\[
dgc = \begin{pmatrix} 1 & 0 & -1 & 0 \\ 0 & 1 & 0 & -1 \end{pmatrix}, \quad \hat{\Gamma}_n = \frac{1}{|T_n|^1}\begin{pmatrix} \hat{\sigma}_n^2 |S_n^0| & \hat{\rho}_n S_n^{0,1} \\ \hat{\rho}_n S_n^{0,1} & \hat{\sigma}_n^2 |S_n^1| \end{pmatrix}.
\]

\[
\hat{\sigma}_n^2 = |T_n|^{-1}\sum_{k\in \Gamma_n} (\hat{e}^2_{2k} + \hat{e}^2_{2k+1}), \quad \hat{\rho}_n = |T_n|^{-1}\sum_{k\in \Gamma_n} \hat{e}_{2k}\hat{e}_{2k+1}, \quad \Gamma_n = \{k \in \mathbb{T}_n: \delta_{2k} = 1\} \text{ and for all } k \in \mathbb{G}_n,
\]

\[
\begin{align*}
\hat{e}_{2k} &= \delta_{2k}(X_{2k} - \hat{a}_n - \hat{b}_n X_k), \\
\hat{e}_{2k+1} &= \delta_{2k+1}(X_{2k+1} - \hat{c}_n - \hat{d}_n X_k).
\end{align*}
\]

Theorem 4.2. Under assumptions (AN.1-2), (AO), (AI) and the null hypothesis \(H_0^2\), one has \((Y_n^f) \overset{L}{\rightarrow} \chi^2(2)\) on \((\mathbb{E}, \mathbb{P}_X)\); and under the alternative hypothesis \(H_1^2\), one has \(\lim_{n\to\infty} |Y_n| = +\infty\) a.s. on \((\mathbb{E}, \mathbb{P}_X)\).

Proof: We mimic the proof of Theorem 3.3 with \(g\) the function defined from from \(\mathbb{R}^4\) onto \(\mathbb{R}^2\) by \(g(x_1, x_2, x_3, x_4) = (x_1 - x_3, x_2 - x_4)^T\), so that \(dgc\) is the gradient of \(g\).

Our second test compares the fixed points \(a/(1-b)\) and \(c/(1-d)\), which are the asymptotic means of \(X_{2k}\) and \(X_{2k+1}\) respectively. Set \(H_0^1\): \(a/(1-b) = c/(1-d)\) the symmetry hypothesis and \(H_1^1\): \(a/(1-b) \neq c/(1-d)\). Let \((Y_n^f)^2\) be the test statistic defined by 
\[
Y_n^f = |T_n|^{-1/2}(\hat{\Delta}_n)^{-1/2}(\hat{a}_n - \hat{b}_n - \hat{c}_n - \hat{d}_n)^T, \quad \text{where} \quad \hat{\Delta}_n = \text{dgf}[T_n^{-1}\Sigma_n^{-1}T_n^{-1}\Sigma_n^{-1}]^{1/2}, \quad \text{dgf} = (1/(1-b), a/(1-b)^2, -1/(1-d), -c/(1-d)^2)^T.
\]

This test statistic has the following asymptotic properties.

Theorem 4.3. Under assumptions (AN.1-2), (AO), (AI) and the null hypothesis \(H_0^1\), one has \((Y_n^f)^2 \overset{L}{\rightarrow} \chi^2(1)\) on \((\mathbb{E}, \mathbb{P}_X)\); and under the alternative hypothesis \(H_1^1\), one has \(\lim_{n\to\infty} |Y_n^f|^2 = +\infty\) a.s. on \((\mathbb{E}, \mathbb{P}_X)\).

Proof: We mimic the proof of Theorem 3.3 with \(g\) the function defined from from \(\mathbb{R}^4\) onto \(\mathbb{R}\) by \(g(x_1, x_2, x_3, x_4) = (x_1/(1-x_2) - x_3/(1-x_4))^T\), so that \(\text{dgf}\) is the gradient of \(g\).

5. Application to simulated data

We now study the behavior of our three tests on simulated data. For each test, we compute, in function of the generation \(n\) and for different thresholds, the proportion of rejections under hypotheses \(H_0^2\) and \(H_1^2\), the latter proportion being an indicator of the power of the test. Proportions are computed on a sample of 1000 replicated trees.

5.1. Asymmetry test for the Galton-Watson process

In Table 1, we see that the observed proportions of p-values under the thresholds (0.05, 0.01, 0.001), are close to the expected proportions of rejection under \(H_0^2\) suggesting that the asymptotic law of the statistic \(|Y_n^f|^2\) is available by generation 8. Under \(H_1^2\), the power of the test increases from 27.8 (%) for the generation 7 to 93.1 (%) for the generation 11 for a risk of type 1 fixed at 0.05.

5.2. Asymmetry tests for the BAR process

The first asymmetry test compares the parameters \((a, c)\) and \((c, d)\). In Table 2, we see that the observed proportions of p-values under the thresholds (0.05, 0.01, 0.001), are close to the expected proportions of rejection under \(H_0^2\) suggesting that the asymptotic law of the statistic \(|Y_n^f|^2\) is available at generation 8. Under \(H_1^2\), the power of the test increases from 37.4 (%) for the generation 7 to 95.7 (%) for the generation 11 for a risk of type 1 fixed at 0.05. For the asymmetry test for the fixed points, we see in Table 3 the observed proportions go away from the expected ones under \(H_0^2\) until the 10th generation, suggesting that the asymptotic law of the statistic is not reached before the 10th generation. We also remark that the power is weak until the 10th generation.
### Table 1: Proportions of p-values under the 0.05, 0.01 and 0.001 thresholds of the asymmetry tests for the means of the GW process (1000 replicas) $p_0 = (0.04, 0.08, 0.08, 0.8)$ (under $H_1$, $p_1 = (0.15, 0.08, 0.08, 0.69)$)

| Generation | Under $H_{GW}^0$ | Under $H_{GW}^1$ |
|------------|------------------|------------------|
|            | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ |
| 7          | 6.4  | 1.9  | 0.3  | 27.8 | 11.8 | 03.6 |
| 8          | 5.6  | 1.4  | 0.3  | 44.2 | 22.2 | 07.6 |
| 9          | 5.5  | 1.1  | 0.3  | 58.6 | 38.5 | 17.0 |
| 10         | 5.7  | 1.5  | 0.2  | 79.4 | 60.8 | 35.9 |
| 11         | 4.8  | 1.0  | 0.1  | 93.1 | 82.0 | 64.2 |

### Table 2: Proportions of p-values under the 0.05, 0.01 and 0.001 thresholds of the asymmetry test for the parameters of the BAR process (1000 replicas) $a = b = 0.5$ (under $H_1$, $c = 0.5; d = 0.4$)

| Gen | Under $H_0^b$ | Under $H_1^b$ |
|-----|----------------|----------------|
|     | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ |
| 7   | 6.6  | 2.2  | 0.6  | 37.4 | 19.7 | 08.0 |
| 8   | 5.5  | 1.5  | 0.3  | 53.6 | 31.0 | 14.6 |
| 9   | 5.5  | 1.3  | 0.3  | 71.1 | 52.3 | 30.3 |
| 10  | 6.3  | 1.2  | 0.1  | 86.8 | 75.5 | 56.1 |
| 11  | 5.9  | 0.6  | 0.1  | 95.7 | 90.8 | 81.4 |

### Table 3: Proportions of p-values under the 0.05, 0.01 and 0.001 thresholds of the asymmetry test for the fixed points of the BAR process (1000 replicas) $a = b = 0.5$ (under $H_1$, $c = 0.5; d = 0.4$)

| Gen | Under $H_0^c$ | Under $H_1^c$ |
|-----|----------------|----------------|
|     | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ | $p < 0.05$ | $p < 0.01$ | $p < 0.001$ |
| 7   | 2.2  | 0.7  | 0    | 23.1 | 07.4 | 01.4 |
| 8   | 3.3  | 0.5  | 0.1  | 41.3 | 20.5 | 06.1 |
| 9   | 3.8  | 0.5  | 0    | 64.6 | 41.6 | 18.6 |
| 10  | 4.7  | 0.8  | 0    | 82.9 | 68.1 | 46.3 |
| 11  | 5.5  | 0.7  | 0.1  | 94.5 | 88.5 | 74.5 |
6. Application to real data: aging detection of Escherichia coli

To study aging in the single cell organism E. coli, [Stewart et al. (2005)](#) filmed 94 colonies of dividing cells, determining the complete lineage and the growth rate of each cell. E. coli is a rod-shaped bacterium that reproduces by dividing in the middle. Each cell inherits an old end or pole from its mother, and creates a new pole. Therefore, each cell has a type: old pole or new pole cell inducing asymmetry in the cell division. [Stewart et al. (2005)](#) propose a statistical study of the genealogy and pair-wise comparison of sister cells assuming independence between the pairs of sister cells which is not verified in the lineage.

Figures 1, 2a, 2b present the results of our tests of the null hypotheses $H_{GW}^0$, $H_c^0$ and $H_f^0$ on the 51 data sets issued of the 94 colonies containing at least eight or nine generations. Figure 1 shows that the hypotheses of equality of the expected number of observed offspring between two sisters is not rejected whatever the data set. This result is not surprising: in our sets, the data are missing most frequently because the cells were out of the range of the camera. The null hypotheses of the two tests on the BAR parameters are rejected for one set in four for $H_c^0$ and for one in eight for $H_f^0$. A global conclusion on the difference between the old pole cell and the new pole cell is not easy. Regarding the results of the simulations in Tables 2 and 3, this lack of evidence is probably due to a low power of the tests at generations 8 and 9. Some data sets with more than 9 generations would probably show a more significant difference.

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