BIOMARKERS FOR HARDI: 2ND & 4TH ORDER TENSOR INVARIANTS

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ABSTRACT

In this paper, we explore the theory of tensor invariants as a mathematical framework for computing new biomarkers for HARDI. We present and explain the *integrity basis*, *basic invariants* and *principal invariants* of 2nd & 4th order tensors to expand on a recently proposed paper on 4th order tensor invariants. We present the mathematical results and compute the basic and principal invariants on a controlled synthetic dataset and an in vivo human dataset. We show how the integrity bases of these two sets of invariants can form a promising framework for developing new biomarkers for HARDI.

***Index Terms*—** HARDI, biomarkers, tensors, integrity basis, basic & principal tensor invariants

1. INTRODUCTION

Biomarkers play an important role in diffusion MRI (dMRI) since they are crucial in detecting and discerning white matter anomalies. Tract based spatial statistics and voxel statistics are computed on biomarkers to study brain connectivity changes related to development, degeneration and disease [1]. Biomarkers in such studies are generally those derived from diffusion tensor imaging (DTI), since DTI is a well established imaging technique that has been widely accepted. Therefore, a number of scalar biomarkers have been proposed for the 2nd order diffusion tensor such as mean diffusivity (MD), fractional anisotropy (FA), relative anisotropy (RA), linear, planar, spherical anisotropies (LA, PA, SA), etc. [2, 3].

However, since DTI is inaccurate in regions with heterogeneous fiber configurations, important higher order models have been proposed to detect fiber crossings with greater accuracy. Although these models have greatly improved tractography, there exist few known biomarkers for such higher order descriptions [4]. The two biomarkers in general use are the generalized anisotropy (GA) [5] and generalized fractional anisotropy (GFA) [6]. It is therefore important to develop new biomarkers for higher order models.

In this paper we explore the theory of 2nd & 4th order tensor invariants as a mathematical framework for computing new biomarkers from higher order models. We are motivated by the fact that most higher order models are either described in the spherical harmonic basis or the Cartesian tensor basis. Since there exists a bijection between these bases [7], biomarkers developed in either of these generalized representations can be computed on a wide gamut of models.

In this paper, we present the concept of the integrity basis for 2nd and 4th order tensors and the two standard bases – the basic invariants and the principal invariants [8]. Our paper expands on [9, 10], which present the principal invariants of the 4th order tensor. We first present these for the 2nd order tensor as an illustration. We then present these bases for the 4th order tensor. We conduct experiments on a controlled synthetic dataset and on an in vivo human dataset where we compute the basic and principal invariants from DTI and "solid-angle" ODFs [11]. These are presented in the results section. We conclude with the idea that these invariants form a promising framework for developing new biomarkers for 4th order spherical harmonic or tensor models

2. MATERIALS AND METHODS

DTI biomarkers such as FA, RA, etc. measure the diffusion anisotropy of the white matter to monitor changes. These biomarkers are computed from the eigenvalues $\lambda_1 \geq \lambda_2 \geq \lambda_3$ of the 2nd order diffusion tensor since the eigenvalues represent properties of the tensor that remain invariant to changes in its matrix representation from coordinate changes. More precisely the eigenvalues of a 2nd order tensor are invariant to rotations of the coordinate system, and form the building blocks for the DTI scalar biomarkers. Therefore, it is important to be able to define, understand and compute the invariants of higher order models under the group of rotations for developing new biomarkers.

Integrity Basis, Basic & Principal invariants: In the theory of (algebraic) invariants of a tensor, an integrity basis is defined as "a set of polynomials, each invariant under a group of transformations, such that any polynomial function invariant under the group is expressible as a polynomial in elements of the integrity basis" [8]. The group of transformations that is of interest to us is the 3D rotation group (although we work with the orthogonal group since it contains the group of 3D rotations). In other words, we would like to find the (polynomial) properties of a tensor that remain invariant under any rotation of the coordinate system. As found in [8], the two standard integrity bases or sets of polynomials invariant under rotations for 2nd & 4th order tensors are the basic invariants (S) and the principal invariants (J). In the following we present these first for the 2nd order diffusion tensor and then for the 4th order tensor, which may represent any higher order model such as the solid-angle ODF.

Invariants of a 2nd order tensor [8]: The problem of finding the rotational invariants of a 2nd order 3D tensor is a classical problem from linear algebra. It boils down to the eigenvalue or spectral decomposition problem of the 3×3 symmetric matrix representation $\mathbf{D}$ of the diffusion tensor. Its solution gives rise to the principal invariants of $\mathbf{D}$. But first we present the *basic invariants* of $\mathbf{D}$, which are defined as

$$\begin{aligned} S2_1 &= \mathrm{tr}(\mathbf{D}) = \lambda_1 + \lambda_2 + \lambda_3 && (1)\\ S2_2 &= \mathrm{tr}(\mathbf{D}^2) = \lambda_1^2 + \lambda_2^2 + \lambda_3^2 && (2)\\ S2_3 &= \mathrm{tr}(\mathbf{D}^3) = \lambda_1^3 + \lambda_2^3 + \lambda_3^3, && (3) \end{aligned}$$

where, as defined earlier, λ_i are the eigenvalues of $\mathbf{D}$. It is easy to verify that $\{S2_i\}$ are invariant under rotations. If $\mathbf{D}$ is transformed to $\mathbf{D}'$ by a 3D rotation $\mathbf{R}$, then in the indexed notation with the Einstein summation convention $D'_{ij} = R_{ik}R_{jl}D_{kl}$. Therefore,

$$\begin{aligned} S2'_1 &= D'_{mm} = R_{mk}R_{ml}D_{kl} = \delta_{kl}D_{kl} = D_{kk} = S2_1 && (4)\\ S2'_2 &= D'_{ik}D'_{ki} = (R_{il}R_{km}D_{lm})(R_{kn}R_{ip}D_{np})\\ &= R_{il}R_{ip}D_{lm}R_{km}R_{kn}D_{np} = \delta_{lp}D_{lm}\delta_{mn}D_{np}\\ &= D_{pm}D_{mp} = S2_2, && (5)\\ S2'_3 &= D'_{ik}D'_{km}D'_{mi}\\ &= (R_{il}R_{kp}D_{lp})(R_{kn}R_{mq}D_{nq})(R_{ms}R_{it}D_{st})\\ &= R_{il}R_{it}D_{lp}R_{kp}R_{kn}D_{nq}R_{mq}R_{ms}D_{st}\\ &= \delta_{lt}D_{lp}\delta_{pn}D_{nq}\delta_{qs}D_{st} = D_{tp}D_{pq}D_{qt} = S2_3. && (6) \end{aligned}$$

The *principal invariants* of $\mathbf{D}$ are defined from its spectral decomposition problem. The eigen-pair of $\mathbf{D}$ can be found by solving its characteristic equation $\det(\mathbf{D} - \lambda\mathbf{I}) = 0$. Since the characteristic equation of $\mathbf{D}$ remains unchanged when $\mathbf{D}$ is transformed by any rotation, its principal invariants are defined as the coefficients of its characteristic polynomial

$$\begin{aligned} J2_1 &= \mathrm{tr}(\mathbf{D}) = \lambda_1 + \lambda_2 + \lambda_3, && (7)\\ J2_2 &= \lambda_1\lambda_2 + \lambda_1\lambda_3 + \lambda_2\lambda_3, && (8)\\ J2_3 &= \det(\mathbf{D}) = \lambda_1\lambda_2\lambda_3. && (9) \end{aligned}$$

Both the basic invariants and the principal invariants form integrity bases for the 2nd order tensor. Therefore, it's possible to relate the two bases and write the elements of one basis as polynomial functions of the other

$$\begin{aligned} J2_1 &= S2_1, && (10)\\ J2_2 &= -\frac{1}{2}(S2_2 - S2_1^2), && (11)\\ J2_3 &= \frac{1}{3}(S2_3 - 3S2_2S2_1 + S2_1^3). && (12) \end{aligned}$$

Invariants of a 4th order tensor [8, 12, 10, 9]: To understand the computation of the 4th order tensor's invariants it is necessary to understand its structure and algebra. If V be a vector space (say $\Re^3$) then the matrix representation $\mathbf{D}$ of a 2nd order tensor can be interpreted as a linear transformation $\mathbf{D} : V \to V$. The space of all linear transformations $\{\mathbf{D}\}$, from V to V, itself forms a vector space $Lin(V)$. A 4th order tensor $\mathcal{A}$ represents a linear transformation from $Lin(V)$ to $Lin(V)$, $\mathcal{A} : Lin(V) \to Lin(V)$. Its operation on a 2nd order tensor of $Lin(V)$ is known as a double contraction, e.g. $\mathbf{C} = C_{ij} = \mathcal{A} : \mathbf{D} = A_{ijkl}D_{kl}$.

However, since $\mathcal{A}$ is a linear transformation, it can also be represented by an appropriate matrix $\mathbf{A}$ and the 2nd order tensor $\mathbf{D} \in Lin(V)$ can be mapped to a vector $\mathbf{d}$. The changes in representations, however, have to be chosen with care to ensure that they preserve the linear transformation, i.e. $\mathcal{A} : \mathbf{D} = \mathbf{A}\mathbf{d}$. A 3D 4th order tensor contains 81 coefficients and can therefore be mapped to a 9×9 matrix, while a 3D 2nd order tensor contains 9 coefficients that can be mapped to a vector in $\Re^9$. However, we only deal with totally symmetric 3D 4th order tensors, ($A_{ijkl} = A_{klij} = A_{jikl} = A_{ijlk}$), which contain 15 coefficients. They operate on symmetric 3D 2nd order tensors $D_{ij} = D_{ji}$, which contain 6 coefficients. These can be mapped to the matrix-vector representations with $\mathbf{d} = [D_{11}, D_{22}, D_{33}, \sqrt{2}D_{12}, \sqrt{2}D_{13}, \sqrt{2}D_{23}]^T$ and Eq.13, which preserve the operation of the linear transformation $\mathcal{A}$. $\mathbf{A}$ is, therefore, a 6×6 symmetric matrix or a 6D 2nd order tensor.

The *basic & principal* invariants of the totally symmetric 3D 4th order tensor $\mathcal{A}$ are defined as the basic and the principal invariants of the 6D 2nd order tensor $\mathbf{A}$. $\mathcal{A}$ has, therefore, 6 basic invariants and 6 principal invariants. These can be computed in terms of ε_i the 6 eigenvalues of $\mathbf{A}$. The basic invariants of $\mathcal{A}$ are

$$\begin{aligned} S4_1 &= \mathrm{tr}(\mathbf{A}) = \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \varepsilon_4 + \varepsilon_5 + \varepsilon_6, && (14)\\ S4_2 &= \mathrm{tr}(\mathbf{A}^2) = \varepsilon_1^2 + \varepsilon_2^2 + \varepsilon_3^2 + \varepsilon_4^2 + \varepsilon_5^2 + \varepsilon_6^2, && (15)\\ S4_3 &= \mathrm{tr}(\mathbf{A}^3) = \varepsilon_1^3 + \varepsilon_2^3 + \varepsilon_3^3 + \varepsilon_4^3 + \varepsilon_5^3 + \varepsilon_6^3, && (16)\\ S4_4 &= \mathrm{tr}(\mathbf{A}^4) = \varepsilon_1^4 + \varepsilon_2^4 + \varepsilon_3^4 + \varepsilon_4^4 + \varepsilon_5^4 + \varepsilon_6^4, && (17)\\ S4_5 &= \mathrm{tr}(\mathbf{A}^5) = \varepsilon_1^5 + \varepsilon_2^5 + \varepsilon_3^5 + \varepsilon_4^5 + \varepsilon_5^5 + \varepsilon_6^5, && (18)\\ S4_6 &= \mathrm{tr}(\mathbf{A}^6) = \varepsilon_1^6 + \varepsilon_2^6 + \varepsilon_3^6 + \varepsilon_4^6 + \varepsilon_5^6 + \varepsilon_6^6, && (19) \end{aligned}$$

and the 6 principal invariants, which as above, are the coefficients of the characteristic equation of $\mathbf{A}$, are

$$\begin{aligned} J4_1 &= \mathrm{tr}(\mathbf{A}) = \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \varepsilon_4 + \varepsilon_5 + \varepsilon_6, && (20)\\ J4_2 &= \varepsilon_1\varepsilon_2 + \varepsilon_1\varepsilon_3 + \varepsilon_1\varepsilon_4 + \varepsilon_1\varepsilon_5 + \varepsilon_1\varepsilon_6\\ &\quad + \varepsilon_2\varepsilon_3 + \varepsilon_2\varepsilon_4 + \varepsilon_2\varepsilon_5 + \varepsilon_2\varepsilon_6 + \varepsilon_3\varepsilon_4 + \varepsilon_3\varepsilon_5\\ &\quad + \varepsilon_3\varepsilon_6 + \varepsilon_4\varepsilon_5 + \varepsilon_4\varepsilon_6 + \varepsilon_5\varepsilon_6, && (21)\\ J4_3 &= \varepsilon_1\varepsilon_2\varepsilon_3 + \varepsilon_1\varepsilon_2\varepsilon_4 + \varepsilon_1\varepsilon_2\varepsilon_5 + \varepsilon_1\varepsilon_2\varepsilon_6\\ &\quad + \varepsilon_1\varepsilon_3\varepsilon_4 + \varepsilon_1\varepsilon_3\varepsilon_5 + \varepsilon_1\varepsilon_3\varepsilon_6 + \varepsilon_1\varepsilon_4\varepsilon_5 + \varepsilon_1\varepsilon_4\varepsilon_6\\ &\quad + \varepsilon_1\varepsilon_5\varepsilon_6 + \varepsilon_2\varepsilon_3\varepsilon_4 + \varepsilon_2\varepsilon_3\varepsilon_5 + \varepsilon_2\varepsilon_3\varepsilon_6 + \varepsilon_2\varepsilon_4\varepsilon_5\\ &\quad + \varepsilon_2\varepsilon_4\varepsilon_6 + \varepsilon_2\varepsilon_5\varepsilon_6 + \varepsilon_3\varepsilon_4\varepsilon_5 + \varepsilon_3\varepsilon_4\varepsilon_6 + \varepsilon_3\varepsilon_5\varepsilon_6\\ &\quad + \varepsilon_4\varepsilon_5\varepsilon_6, && (22) \end{aligned}$$

$$\mathbf{A} = \begin{pmatrix} A_{1111} & A_{1122} & A_{1133} & \sqrt{2}A_{1112} & \sqrt{2}A_{1113} & \sqrt{2}A_{1123} \\ A_{1122} & A_{2222} & A_{2233} & \sqrt{2}A_{2212} & \sqrt{2}A_{2213} & \sqrt{2}A_{2223} \\ A_{1133} & A_{2233} & A_{3333} & \sqrt{2}A_{3312} & \sqrt{2}A_{3313} & \sqrt{2}A_{3323} \\ \sqrt{2}A_{1112} & \sqrt{2}A_{2212} & \sqrt{2}A_{3312} & 2A_{1122} & 2A_{1123} & 2A_{2213} \\ \sqrt{2}A_{1113} & \sqrt{2}A_{2213} & \sqrt{2}A_{3313} & 2A_{1123} & 2A_{1133} & 2A_{3312} \\ \sqrt{2}A_{1123} & \sqrt{2}A_{2223} & \sqrt{2}A_{3323} & 2A_{2213} & 2A_{3312} & 2A_{2233} \end{pmatrix}. \quad (13)$$

$$\begin{aligned} J4_4 &= \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4 + \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_5 + \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_6 + \varepsilon_1\varepsilon_2\varepsilon_4\varepsilon_5 \\ &\quad + \varepsilon_1\varepsilon_2\varepsilon_4\varepsilon_6 + \varepsilon_1\varepsilon_2\varepsilon_5\varepsilon_6 + \varepsilon_1\varepsilon_3\varepsilon_4\varepsilon_5 + \varepsilon_1\varepsilon_3\varepsilon_4\varepsilon_6 \\ &\quad + \varepsilon_1\varepsilon_3\varepsilon_5\varepsilon_6 + \varepsilon_1\varepsilon_4\varepsilon_5\varepsilon_6 + \varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_5 + \varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_6 \\ &\quad + \varepsilon_2\varepsilon_3\varepsilon_5\varepsilon_6 + \varepsilon_2\varepsilon_4\varepsilon_5\varepsilon_6 + \varepsilon_3\varepsilon_4\varepsilon_5\varepsilon_6, & (23) \\ J4_5 &= \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_5 + \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_6 + \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_5\varepsilon_6 + \\ &\quad \varepsilon_1\varepsilon_2\varepsilon_4\varepsilon_5\varepsilon_6 + \varepsilon_1\varepsilon_3\varepsilon_4\varepsilon_5\varepsilon_6 + \varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_5\varepsilon_6, & (24) \\ J4_6 &= \det(\mathbf{A}) = \varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4\varepsilon_5\varepsilon_6. & (25) \end{aligned}$$

Verifying the invariance to rotation of these two integrity bases of $\mathcal{A}$ is not straightforward. By the same arguments as Eqs. 4,5,6, and the argument of the characteristic equation it is simple to show that the invariants of $\mathcal{A}$ or $\mathbf{A}$ are invariant to rotations in $\Re^{6\times6}$. It can be shown that rotations in $\Re^{3\times3}$ can be mapped to a subgroup of rotations in $\Re^{6\times6}$ [13], therefore the basic & principal invariants of $\mathcal{A}$ ($\mathbf{A}$) are invariant to 3D rotations. However, since these were computed as invariants to 6D rotations, we suspect that there should exist up to 12 invariants of $\mathcal{A}$ that are invariant only to 3D rotations. (A 3D rotation can be represented by 3 coefficients and $\mathcal{A}$ has 15). We are exploring these currently in our ongoing research.

As for the 2nd order tensor, it is also possible to relate the basic & principal invariants of the 4th order tensor.

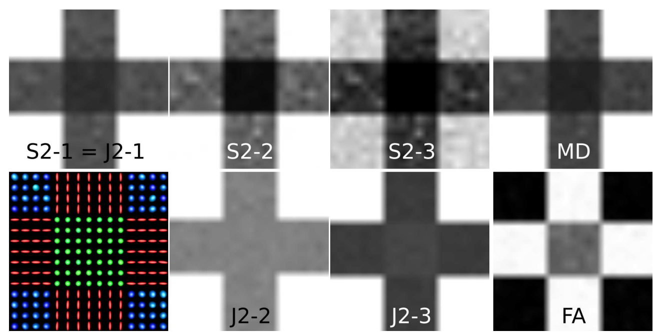
3. EXPERIMENTS AND RESULTS

First, we conduct experiments on a controlled synthetic dataset. The diffusion signal for a voxel was generated using $S(\mathbf{g}_i) = \sum_{k=1}^{M} \exp\left(-b\mathbf{g}_i^T \mathbf{D}_k \mathbf{g}_i\right)$ for M fibers (1 or 2) with $\mathbf{D}_k = \mathbf{R}_k^T \mathrm{diag}(1390, 355, 355)\mathbf{R}_k \times 10^{-6} mm^2/s$ where $\mathbf{R}_k$ are appropriate 3D rotations. Isotropic voxels were created using $\mathbf{D} = \mathrm{diag}(700, 700, 700)\ \times 10^{-6} mm^2/s$. Then we conduct experiments on an in vivo human brain dataset [14]. It was acquired on a 3T Siemens scanner, with 60 gradient directions and a b-value of $1000 s/mm^2$.

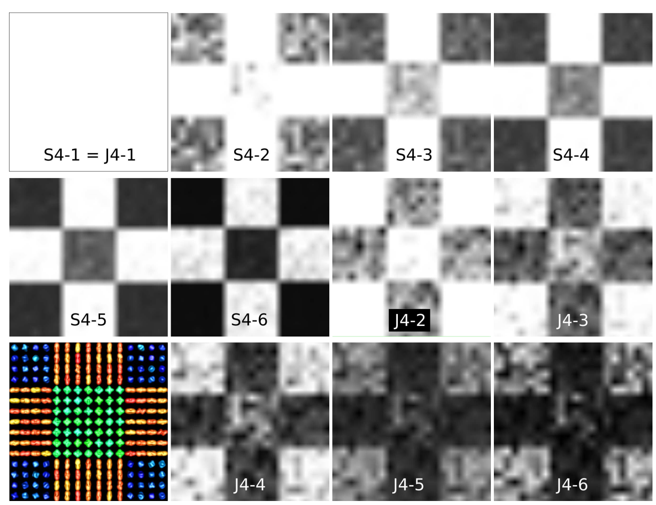
Fig.1 shows the results from the synthetic dataset. In Fig.1a. are shown the 3 basic ($S2_i$) and 3 principal ($J2_i$) invariants computed from the DTI estimation of the signal. For comparison the MD & FA are also shown. In Fig.1b. are shown the 6 basic ($S4_i$) and 6 principal ($J4_i$) invariants computed from the rank-4 ODF estimation [11] of the signal. Clearly the integrity basis seems to capture more information than single scalars like the FA or MD in both the DTI & ODF.

Fig.2 shows the 6 basic ($S4_i$) and 6 principal ($J4_i$) invariants computed from the rank-4 ODF estimation [11] from the in vivo human dataset. The GFA is also shown for comparison. Again the two sets of invariants of the 4th order tensor's integrity basis seem to capture more detailed information.

These results strongly indicate that the integrity basis for 2nd & 4th order tensors form a promising framework for developing new biomarkers for HARDI. These different invariants can be combined to create different scalar measures that can be employed as biomarkers to discern white matter changes or anomalies.



(a) DTI Basic & Principal invariants.



(b) Solid-angle ODF Basic & Principal invariants.

Fig. 1. Basic & Principal invariants (a) from DTI estimated from a multi-tensor based synthetic dataset simulating isotropic, single fiber and two fiber crossing voxels, (b) from rank-4 solid-angle ODFs [11]. For comparison the MD & FA are also presented.

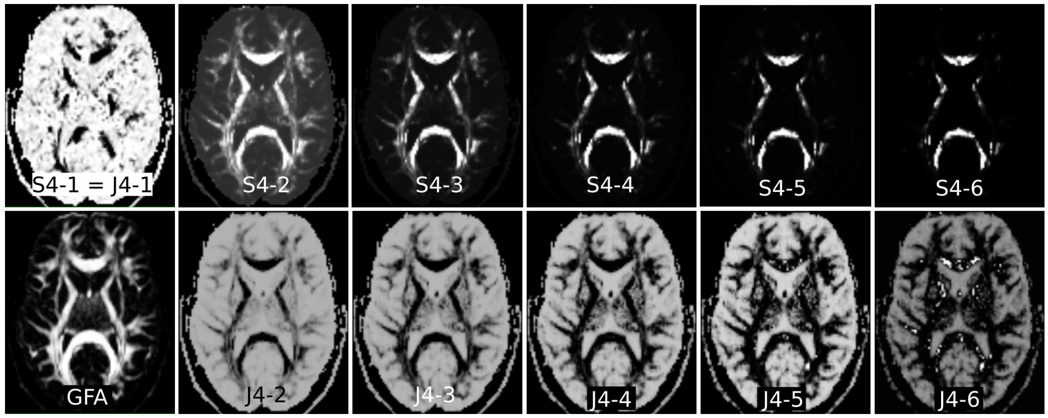


Fig. 2. Basic & Principal invariants from rank-4 solid-angle ODFs [11] estimated from an in vivo human dataset (axial slice). For comparison the GFA [6] is also presented.

4. CONCLUSION

We explored the theory of tensor invariants and presented the concepts of the integrity basis, basic invariants and principal invariants for 2nd & 4th order tensors. We presented their mathematical formulae and results. We computed these for 2nd & 4th order tensors on a controlled synthetic dataset and an in vivo human dataset. Although the integrity basis for the 2nd order tensor are the true 3D rotation invariants, we suspect that more 3D rotation invariants exist for the 4th order tensor. Nonetheless, the integrity bases provide a promising mathematical framework for developing new biomarkers for HARDI.

5. REFERENCES

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