Algebraic constraints on the transition probability matrices produced from Lie-Markov models

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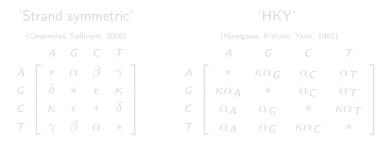
Some algebraic definitions

- Take L ⊆ Mat_n(ℝ) to be a linear subspace of matrices i.e. A, B ∈ L ⇒ A + λB ∈ L
- L is an 'algebra' if it is closed under a 'product' (binary operation):
- (i.) Matrix algebra: $AB \in \mathcal{L}$
- (ii.) Lie algebra: $[A, B] := AB BA \in \mathcal{L}$
- (ii.) Jordan algebra: $\{A, B\} := AB + BA \in \mathcal{L}$

(Were 'AB' is the usual matrix product we all know and love!)

Continuous time Markov chains for DNA evolution

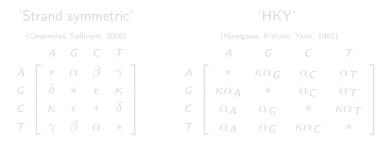
▶ Generator matrix Q → P = e^{Qt}, transition matrix
 ▶ Exemplar DNA (A,G,C,T) models:



- Strand symmetric: rate $(A \rightarrow G) = rate(T \rightarrow C)$
- HKY: κ is the 'transition/transversion' ratio (AG/CT)

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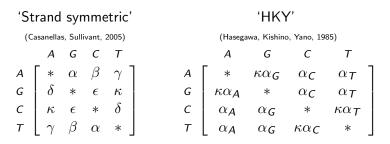


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 ▶ Transition matrices are multiplicative: (P₁, P₂) → P₁P₂ But what about a particular model?
 ▶ If P₁ = e^{Qt₁} and P₂ = e^{Qt₂} then P₁P₂ = e^{Q(t₁+t₂)}

i.e. same transition rates, longer time

If the transition rates change:

Commuting case: $Q_1 Q_2 = Q_2 Q_1$,

$$P_1 P_2 = e^{Q_1 t_1} e^{Q_2 t_2} = e^{Q_1 t_1 + Q_2 t_2}$$

General case:

 $P_1P_2 = e^{Q_1t_1}e^{Q_2t_2} = e^{Q_1t_1+Q_2t_2+(\text{infinite series of corrections})}$ $= e^{Q_1t_1+Q_2t_2+\frac{1}{2}t_1t_2[Q_1,Q_2]+\dots}$

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Some models are multiplicative closed, some are not

Necessary and sufficient condition for closure (roughly): generators span a Lie algebra *L* : *Q*₁ + λ*Q*₂ and [*Q*₁, *Q*₂] ∈ *L*

Strand-symm model is closed because the products $Q_1Q_2 \in \mathcal{L}$:

 $Q_1Q_2, Q_2Q_1 \in \mathcal{L}$ (and linearity) $\implies [Q_1, Q_2] = Q_1Q_2 - Q_2Q_1 \in \mathcal{L}$

So some models form matrix algebras and we observe:

matrix algebra \implies Lie algebra \iff mult. closed

► HKY is not closed because it is non-linear:

$$Q = \begin{pmatrix} * & \kappa \alpha_G & \alpha_C & \alpha_T \\ \kappa \alpha_A & * & \alpha_C & \alpha_T \\ \alpha_A & \alpha_G & * & \kappa \alpha_T \\ \alpha_A & \alpha_G & \kappa \alpha_C & * \end{pmatrix} \implies Q_{12}Q_{13} = Q_{43}Q_{42}, \text{ etc}$$

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Structure of models that form matrix algebras

A model where the generators span a matrix algebra is always closed:

$$e^Q = \mathcal{I} + (Q + Q^2/2 + \ldots) = \mathcal{I} + \hat{Q}$$

 $\implies e^{Q_1} e^{Q_2} = (\mathcal{I} + \hat{Q_1})(\mathcal{I} + \hat{Q_2}) = \mathcal{I} + \left(\hat{Q_1} + \hat{Q_2} + \hat{Q_1}\hat{Q_2}\right)$

i.e. closure under sums and products is sufficient (although the latter is not necessary...)

Easy to infer the structure of the transition matrices:

$$\mathcal{M} = \mathcal{I} + \mathcal{L}$$

i.e. "transition matrix = $\mathcal{I}+$ generator"

Examples include most of the known multiplicatively closed DNA models we know of (e.g. group-based)

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• e.g., symmetric generators do not form a Lie algebra: $(Q_1Q_2)^T = Q_2^T Q_1^T = Q_2 Q_1 \neq Q_1 Q_2$ and $[Q_1, Q_2]^T = -[Q_1, Q_2]$

However,

$$(Q^2)^T = Q^2, \quad (Q^3)^T = Q^3 \dots$$

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Not all multiplicatively closed models satisfy " $\mathcal{M} = \mathcal{I} + \mathcal{L}$ "

Toy model L:

$$Q=egin{pmatrix} st & lpha+eta & 2eta\ 0 & 0 & 0\ 2lpha & lpha+eta & st \end{pmatrix}$$

 $\begin{array}{l} \mbox{Intentionally designed so } [\mathcal{Q}_1,\mathcal{Q}_2] \in \mathcal{L} \mbox{ but } \mathcal{Q}_1\mathcal{Q}_2 \notin \mathcal{L} \\ \implies \mathcal{M} \neq \mathcal{I} + \mathcal{L} \end{array}$

 \blacktriangleright This Lie algebra is "algebraic" $\implies \mathcal{M}$ has an algebraic description:

$$e^Q \sim P = egin{pmatrix} * & a & z \ 0 & 1 & 0 \ y & a & * \end{pmatrix}, ext{ with } y + z - a(a-1)(a-2) = 0$$

In general these non-linear constraints are difficult to find and they are not always algebraic. (de Graff, Adriaan, 2017) Not all multiplicatively closed models satisfy " $\mathcal{M}=\mathcal{I}+\mathcal{L}$ "

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- Require linearity plus closure under powers.
- Jordan algebra J: linearity and {A, B} = AB + BA ∈ J.
 Equivalent to closure under powers: A² = ¹/₂(AA + AA) and (A + B)² = A² + (AB + BA) + B²
- Symmetric case:

 $(Q_1Q_2 + Q_2Q_1)^T = Q_2^TQ_1^T + Q_1^TQ_2^T = Q_2Q_1 + Q_1Q_2 = Q_1Q_2 + Q_2Q_1$

If we demand **both** the Lie and Jordan conditions, we obtain precisely a the matrix algebra case:

$$AB = \frac{1}{2}[A, B] + \frac{1}{2}\{A, B\}$$

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The end

- Efficient computations of matrix exponentials?
 - e.g. decompose relevant algebra into irreducible components
- Direct parametrisation of transition matrices?
 - i.e. bypass matrix exponentials altogether
- Insights into why certain results are provable for some models but not others? e.g. the equal-input model

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