Dear Colleagues,

Thank you very much for your valuable comments and suggestions.

Based on our recent theoretical studies of spectral mirror symmetry (DOI: 10.13140/RG.2.2.19473.90724) we performed a substantial (major) revision of the manuscript.

It has become clear that the balance of resonance frequencies is a crucial condition, meaning that spins must be ordered by their resonance frequencies (ascending or descending), and the symmetry of the J-coupling matrix should be investigated in this order. We also established rules for the additional ordering of chemically equivalent but magnetically nonequivalent spins. These results have been incorporated into the revised text of the manuscript.

A detailed, point-by-point response to all of the reviewers' comments is provided below.

Comments from Michael Tayler:

> This manuscript reports an interesting symmetry theorem for high-field NMR,
> which I admit I didn't know of before, but think is useful to describe to
> community. The theorem is well explained, and although perhaps lacking a
> rigorous "proof", it is enough to be convincing. Some minor comments for
> improvement:
> (1) The authors should use existing terminology for the matrices -- a
> matrix that is symmetric about it's secondary diagonal is called a
> persymmetric matrix, which, indeed, has known connections to permutation
> matrices/operators, see https://en.wikipedia.org/wiki/Persymmetric_matrix,

The term 'persymmetric matrix' has been incorporated into the text where appropriate.

> and (2) the theorem implicitly relies on spin eigenstates that are Zeeman
> product states. One must therefore state that the rule breaks down in low
> fields, for example, in the molecules containing 1H-19F coupled spins at
> fields comparable to or weaker than earth's field.

You are absolutely right. This clarification has been added to the text.

Comments from Norbert Mueller:

> The authors address a topic that has not been given much attention in the
> recent literature, the relation between symmetry of NMR-spectra and symmetry
> of molecules. This may erroneously be believed to be a trivial problem,
> but clearly may range from deceptively simple to highly complex. While the
> symmetry of first order multiplets is a well-understood fact, the case(s)
> of symmetry with respect to the entire spectrum proves to be a more
> intricate problem. The authors provide two criteria: (1) Unsurprisingly,
> the frequency distribution around the center frequency must be symmetric,
> (2) the symmetry of the J-coupling matrix with respect to what the authors
> call secondary diagonal is presented as the necessary condition for
> spectral symmetry.

The term 'secondary diagonal' has been replaced by the more precise term 'anti-diagonal'.

> There is not much current literature pertaining to this topic. The book by
> Corio, which is mentioned in comments on the MR web-site, would surely
> help. I tried for a week to get hold of a copy but failed. There is one

> related paper by Corio (Journal of Chemical Education, Volume 46, Number 6,
> June 1969) but it highlights only aspects (e.g. AA BB systems) of what
> could be found in that book. But it would be worth comparing the results.

The mentioned Corio article (J.Chem.Educ., 1969, 46(6), 345-350,
DOI: 10.1021/ed046p345) is devoted to the composite particle approach for
simulating spectra of spin systems containing magnetically equivalent spin
groups. However, it does not contain a description of the AA'BB' (AA'XX')
spin system, nor does it address the issue of NMR spectral symmetry.

A reference to the "Symmetry Theorem for AnBn Systems" on page 254 of
the Corio monograph has been added to the text.

> Note: I believe Mohamed Sabba (U. of Southampton) recently did some highly
> advanced work on coupling networks, dealing with simulations of large
> complicated spin systems. He has some novel approaches on his blog
> (https://arxiv.org/html/2404.03560v2) and may be the right person to propose
> improvements to the approaches of the current paper. I am not completely
> certain but he posted some impressive simulations on what used to be
> twitter . Dr. Sabba s work does not address exactly the cases the authors
> consider but may lead to a more elegant general solution. Also the aspect
> of dynamics needs to be addressed or at least it should be clearly stated
> that this approach is (or is not) applicable in cases of dynamic averaging
> of spin system parameters.

The reasoning in the manuscript and the spectral simulations are based on the
high-resolution spin Hamiltonian formalism, which implies a stationary picture
with dynamically averaged parameters of the spin system.

> Reviewers conclusion: The paper draws attention to an important overlooked
> question, which maybe relevant also in the context of QIP (quantum
> information processing) and proposes a solution. But it seems a bit
> incomplete, an elegant mathematical or algorithmic solution to the ordering
> of the coupling matrix elements is missing, in my humble opinion.
> Nevertheless I recommend it for publication after revision, so as to
> provide a basis for continued deliberation of this topic by this and other
> research groups.

Based on our recent theoretical studies (DOI: 10.13140/RG.2.2.19473.90724),
it seems that we have found the optimal way to order spins. Spins should be
monotonically ordered by resonance frequencies, the order of magnetically
equivalent spins is unimportant, chemically equivalent but magnetically
nonequivalent spins should be ordered in such a way that
JAX=JA'X'=JA''X''=JA'''X''' (spin subsystems topologically consistent order).

> Addressing the formal criteria required for a review report:
> Scientific impact: good
> Scientific quality: OK, there is some lack of mathematical rigor, see comments
> by Michael Tayler and Tom Barbara on the MR-website..
> Novelty: OK, but the AA BB system simulations have been around for some time.
> Presentation quality: OK, room for improvement, the figure captions could be
> more informative
> The language could be improved by some native speaker s expertise.
> Additional references as mentioned in this review and by the commenters on
> the MR-website should be added.
> So, I recommend a major revision.

The above comments have been addressed in the revised version of the
manuscript.