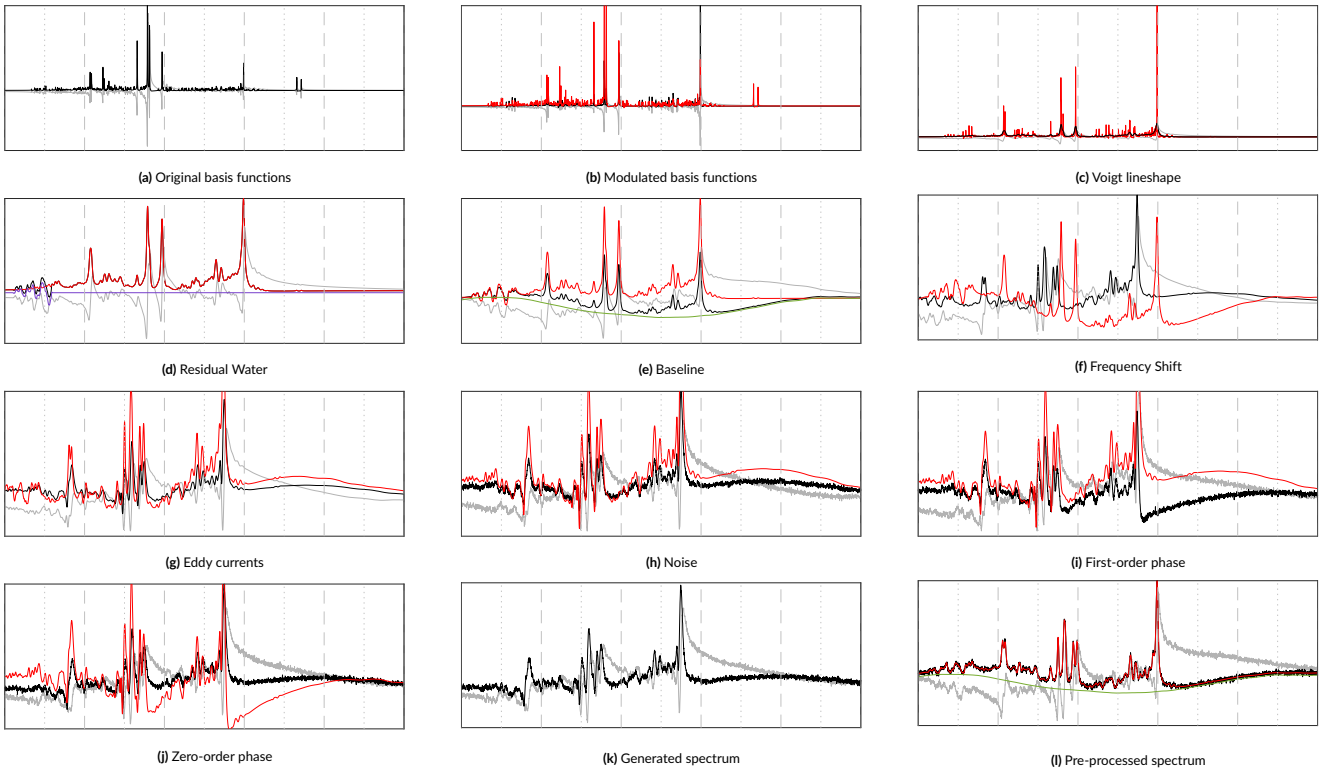

FIGURE 1 This is a step-by-step progression through the physics model. The real and imaginary components are in black and grey, respectively. The red line includes only the metabolites and the offsets from the preceeding steps. 1k is the final spectrum with all artifacts applied. 1l is the pre-processed spectrum with the phase and frequency shifts removed.

2.1.2 | Basis Functions

MRI, and its derivatives, are spatially resolved imaging modalities. Even singular pixels in MRI images represent a 3D volume with a spatial distribution, as shown in Fig. 2a. Addressing this spatial component is important when working with quantitative MR modalities like spectroscopy. Inaccurately simulated basis functions cause errors in metabolite quantification when fitting in vivo data. With simulated data, such basis functions negatively impact the realism of the simulations, limiting their usefulness, especially for validating quantitative methods.

The importance of considering spatial localization led to Landheer *et al.*'s MARSS[23] software package being selected for the default basis functions provided with this simulator. MARSS produces high-fidelity outputs by simulating 128 points in each direction. This very accurately captures the spatial nature of MR imaging. MARSS has a large number of common brain metabolites already defined in their template files. Vendor-specific basis functions for these metabolites can be simulated with PRESS and STEAM sequences. Custom basis functions can also be simulated with various metabolites, T1 and T2 relaxations, and specialized pulse sequences, e.g. editing sequences, (semi-)Laser, etc.

Macromolecules and Lipids

Current spectral fitting methods for modeling MM and lipid signals are based on creating a group of curves that resemble clinical data but are not informed by any underlying physical phenomenon. Each fitting package contains their own set of basis functions for modeling these regions. Until this knowledge gap is filled in, this work uses pre-generated basis functions from Osprey[36] that were resampled to match the simulated basis functions from MARSS.

2.1.3 | Amplitude Modulation

Metabolite quantities produced during spectral fitting are of an arbitrary scale. Comparing these quantities with a standard reference puts them into context. In vivo proton scans generally use an internal reference metabolite for relative quantification. Creatine is the default metabolite because its concentration is relatively stable. As a result, concentrations maps are generally reported as ratios with respect to creatine and all amplitude values in this model are defined *wrt* creatine as the default. For this framework, physiological values were derived from work by Das *et al.*[18,34].