Applicability analysis of validation evidence for biomedical computational models

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Computational modelling has the potential to revolutionise medicine the way that it transformed physics and engineering, but despite decades of work there has been limited progress to successfully translate research to patient care. One major difficulty with biomedical models is often an inability to perform validation in a setting that closely resembles how the model will be used. For example, for a model that makes in vivo clinical predictions, 'direct validation' of predictions may be impossible for ethical, technological or financial reasons. The unavoidable difference between how a biomedical model may be validated versus how it is used, can lead to difficulty in rigorously assessing validation evidence, and lack of trust in biomedical models. While the engineering literature provides some guidance regarding 'applicability' – whether validation evidence supports the model for a specific context of use (COU) – current methods are motivated by engineering problems and not very relevant to biomedical problems. We propose a novel framework for performing applicability analysis, that is, the systematic assessment of the applicability of a computational model to a COU given the validation evidence. The framework provides a step-by-step method for breaking down the broad question of applicability into a series of tractable questions. The proposed framework is relevant to a wide range of biomedical models and models from other disciplines, and a wide range of underlying physics.