Abstract: Locality and separability of the potential energy of a molecular system (I will focus on materials) is the implicit premise of molecular mechanics and of virtually all multi-scale methods. A classical, and well-understood example, is the locality of the density matrix. This notion of locality is insufficient to justify multi-scale algorithms. In this talk, I will show in detail how the required locality of forces and potential energy arises in some simple electronic structure models. I will then exploit these results in the construction of new interatomic potentials and QM/MM multi-scale algorithms with rigorous rates of convergence in terms of the QM region size.