We ask when embedding calculus can distinguish pairs of smooth manifolds that are homeomorphic but not diffeomorphic. We prove that, in dimension 4, the answer is “almost never”. In contrast, we exhibit an infinite list of high-dimensional exotic spheres detected by embedding calculus. The former result implies that the algebraic topology of knot spaces is insensitive to smooth structure in dimension 4, answering a question of Viro. The latter result gives a partial answer to a question of Francis and hints at the possibility of a new classification of exotic spheres in terms of a stratified obstruction theory applied to compactified configuration spaces. This talk represents joint work with Alexander Kupers.